Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Phenacyl azides as efficient intermediates: One-pot synthesis of pyrrolidines and imidazoles

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List of contents

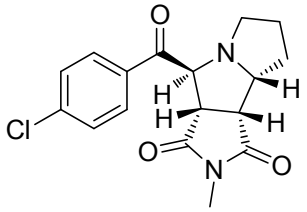
General

The reagents, chemicals and solvents were either purchased from commercial suppliers or prepared and purified by standard techniques. Column chromatography was carried out using silica gel 100-200 mesh. Infrared spectra were recorded using a FT-IR spectrophotometer and values reported in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded with 300 and 500 MHzNMR instruments with tertramethylsilane (TMS) as an internal standard. High-resolution mass spectra (ESI-HRMS) were recorded on ESI-QTOP mass spectrometer.

Typical experimental procedure for three component coupling of phenacyl azides, secondary amino acids (L-proline, L-thioproline, and pipecolic acid), and maleimides (compounds 4a-l).

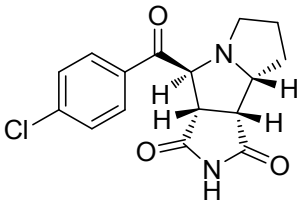
To a 25 mL round bottom flask, phenacyl azide (1.1 mmol), secondary amino acids (1 mmol), maleimide (1.1 mmol), Et_3N (1 mmol), methanol (15 mL) were added and the reaction mixture was refluxed in air for 12 h. Next the reaction solvent was evaporated to yield a crude reaction product which was purified using silica-gel column chromatography to yield desired products (**5a-l**).

4-(4-Chlorobenzoyl)-2-methylhexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4a).



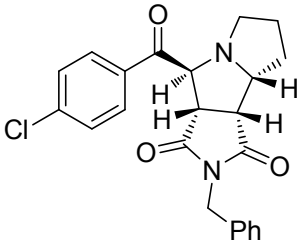
Yellow solid; 156 mg (77%); mp:165−167 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 5.08 (s, 1H), 3.92 (d, J = 8.2 Hz, 1H), 3.79–3.75 (m, 1H), 3.40–3.31 (m, 2H), 2.99 (s, 3H), 2.53 (dd, J = 16.3, 8.9 Hz, 1H), 2.26 (ddd, J = 10.9, 6.6, 3.6 Hz, 1H), 2.04 (dt, J = 16.5, 7.8 Hz, 1H), 1.94–1.76 (m, 1H), 1.60 (ddd, J = 13.0, 10.8, 6.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.9, 179.4, 177.8, 139.9, 133.0, 130.6, 129.0, 70.8, 66.6, 54.2, 49.6, 49.3, 25.9, 25.3, 24.6; IR (KBr, cm^{-1}): 2928, 2835, 1767, 1694, 1586, 1429, 1377, 1277, 1227; ESI-HRMS calcd for $C_{17}H_{18}ClN_2O_3$ 333.1006 $[M+H]^+$, found 333.1009.

4-(4-Chlorobenzoyl)hexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4b).



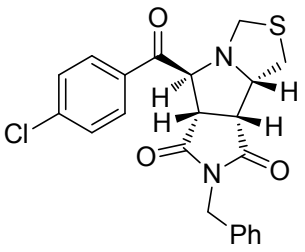
Yellow solid; 127 mg (70%); mp: 208−210 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO) δ 10.97 (s, 1H), 8.03 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 5.07 (s, 1H), 3.88 (dd, *J* = 8.4, 1.0 Hz, 1H), 3.80–3.66 (m, 1H), 3.33 (dt, *J* = 17.9, 8.2 Hz, 2H), 2.74 (dd, *J*= 17.2, 8.0 Hz, 1H), 2.36–2.19 (m, 1H), 2.13 – 1.95 (m, 1H), 1.93 – 1.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO) δ 198.6, 184.9, 183.6, 144.4, 137.7, 135.4, 133.7, 75.3, 71.6, 58.9, 55.3, 55.2, 30.6, 29.5. IR (KBr, cm^{-1}): 2925, 1709, 1589, 1337, 1241, 1197; ESI-HRMS: calcd for $C_{16}H_{16}ClN_2O_3$ 319.0849 $[M+H]^+$, found 319.0847.

2-Benzyl-4-(4-chlorobenzoyl)hexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4c).



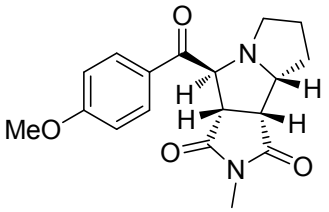
White solid; 184 mg (75%); mp: 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.6 Hz, 2H), 7.46-7.42 (m, *J* = 7.4, 4.9, 1.9 Hz, 4H), 7.35–7.27 (m, 3H), 5.01 (s, 1H), 4.67 (d, *J* = 13.7 Hz, 1H), 4.62 (d, *J* = 13.7 Hz, 1H), 3.90 (dd, *J* = 8.3, 0.9 Hz, 1H), 3.81 – 3.67 (m, 1H), 3.34 (t, *J* = 8.8 Hz, 1H), 3.09 (td, *J* = 8.7, 4.4 Hz, 1H), 2.17–2.00 (m, 2H), 1.97–1.86 (m, 1H), 1.62–1.49 (m, 1H), 1.17–1.02 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 179.0, 177.3, 139.9, 134.7, 133.0, 130.5, 129.4, 129.0, 128.7, 128.3, 70.7, 66.6, 53.8, 49.6, 49.3, 42.9, 25.3, 24.1. IR (KBr, cm^{-1}): 2926, 2806, 1769, 1698, 1588, 1397, 1345, 1235; ESI- HRMS: calcd for $C_{23}H_{22}ClN_2O_3$ 409.1319 $[M+H]^+$, found 409.1319.

7-Benzyl-5-(4-chlorobenzoyl)tetrahydro-3*H*-pyrrolo[3',4':3,4]pyrrolo[1,2-*c*]thiazole-6,8(1*H*,7*H*)-dione (4d).



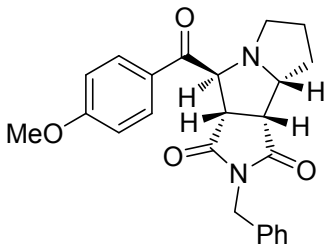
White solid; 192 mg (75%); mp: 175−177 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.39 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.36–7.27 (m, 3H), 4.88 (d, *J* = 3.9 Hz, 1H), 4.64 (s, 2H), 4.24 (d, *J* = 9.8 Hz, 1H), 4.08–3.97 (m, 1H), 3.81 (d, *J* = 9.8 Hz, 1H), 3.76 (dd, *J* = 8.9, 3.9 Hz, 1H), 3.61 (t, *J* = 8.8 Hz, 1H), 3.02 (dd, *J* = 11.7, 6.4 Hz, 1H), 2.91 (dd, *J* = 11.7, 4.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.6, 177.2, 175.3, 140.6, 135.1, 133.3, 130.6, 129.3, 129.1, 128.7, 128.2, 69.5, 68.9, 58.0, 49.4, 48.3, 43.1, 33.1; IR (KBr, cm^{-1}): 2927, 2854, 1766, 1685, 1584, 1489, 1423, 1339, 1342, 1227; ESI-HRMS: calcd for $C_{22}H_{20}ClN_2O_3S$ 427.0883 $[M+H]^+$, found 427.0875.

4-(4-Methoxybenzoyl)-2-methylhexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4e).



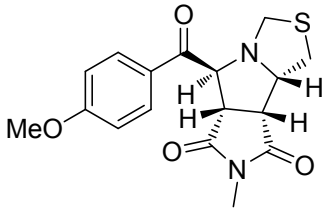
White solid; 134 mg (71%); mp: 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 5.11 (s, 1H), 4.03–3.73 (m, 5H), 3.44 –3.24 (m, 2H), 2.98 (s, 3H), 2.52 (dd, *J* = 16.4, 8.9 Hz, 1H), 2.34–2.19 (m, 1H), 2.05 (dt, *J* = 21.1, 7.6 Hz, 1H), 1.94–1.75 (m, 1H), 1.70–1.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 179.8, 178.1, 163.8, 131.5, 127.6, 113.9, 70.6, 66.6, 55.5, 54.1, 49.7, 49.6, 25.8, 25.2, 24.6; IR (KBr, cm^{-1}): 2961, 2818, 1770, 1697, 1672, 1603, 1509, 1436, 1266; ESI-HRMS: calcd for $C_{18}H_{21}N_2O_4$ 329.1501 $[M+H]^+$, found 329.1501.

2-Benzyl-4-(4-methoxybenzoyl)hexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4f).



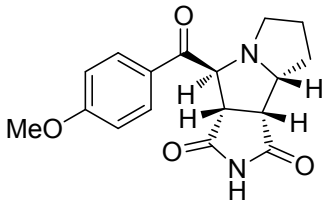
White solid; 177 mg (74%); mp: 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 9.0 Hz, 2H), 7.43 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.38–7.27 (m, 3H), 6.95 (d, *J* = 9.0 Hz, 2H), 5.05 (s, 1H), 4.67 (d, *J* = 13.7 Hz, 1H), 4.62 (d, *J* = 13.7 Hz, 1H), 3.90–3.88 (m, 4H), 3.84–3.74 (m, 1H), 3.42–3.29 (m, 1H), 3.10 (td, *J* = 8.6, 4.3 Hz, 1H), 2.17–1.87 (m, 2H), 1.57 (dqd, *J* = 9.7, 8.2, 5.6 Hz, 1H), 1.10 (qdd, *J* = 19.9, 9.9, 5.6 Hz, 1H), 0.94–0.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 179.2, 177.5, 163. 8, 134.8, 131.5, 129.4, 128.6, 128.2, 127.5, 113.9, 70.5, 66.7, 55.5, 53.8, 49.7, 49.7, 42.9, 25.3, 24.1; IR (KBr, cm^{-1}): 2963, 1771, 1698, 1676, 1598, 1510, 1392, 1257; ESI-HRMS: calcd for $C_{24}H_{25}N_2O_4$ 405.1814 $[M+H]^+$, found 405.1802.

5-(4-Methoxybenzoyl)-7-methyltetrahydro-3*H*-pyrrolo[3',4':3,4]pyrrolo[1,2-*c*]thiazole-6,8(1*H*,7*H*)-dione (4g).



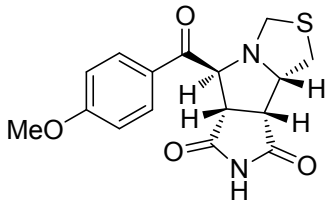
White solid; 204 mg (89%); mp: 154−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 4.96 (d, *J* = 3.8 Hz, 1H), 4.30 (d, *J* = 9.8 Hz, 1H), 4.08 (dt, *J* = 8.4, 5.7 Hz, 1H), 3.92 (d, *J* = 9.9 Hz, 1H), 3.90 (s, 3H), 3.80 (dd, *J* = 8.8, 3.8 Hz, 1H), 3.63 (t, *J* = 8.7 Hz, 1H), 3.12 (dd, *J* = 11.7, 6.2 Hz, 1H), 3.07–2.89 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 177.8, 176.1, 164.3, 131.6, 127.9, 114.2, 69.5, 68.6, 58.1, 55.6, 49.7, 48.6, 33.6, 25.3; IR (KBr, cm^{-1}): 2952, 2872, 1777, 1706, 1668, 1597, 1569, 1428, 1268; ESI-HRMS: calcd for $C_{17}H_{19}N_2O_4S$ 347.1066 $[M+H]^+$, found 347.1063.

4-(4-Methoxybenzoyl)hexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4h).



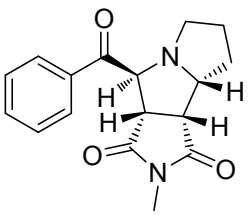
White solid; 157 mg (80%); mp: 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.9 Hz, 2H),7.94 (s, 1H), 6.97 (d, *J* = 8.9 Hz, 2H), 5.13 (s, 1H), 3.97 (dd, *J* = 8.5, 1.2 Hz, 1H), 3.93–3.68 (m, 4H), 3.38 (ddd, *J* = 10.7, 9.4, 6.8 Hz, 2H), 2.73 (dd, *J* = 17.4, 8.1 Hz, 1H), 2.36 – 2.21 (m, 1H), 2.15–2.01 (m, 1H), 1.85 (ddq, *J* = 12.9, 9.2, 5.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO) δ 198.7, 185.5, 184.1, 168.5, 136.4, 132.4, 118.9, 74.9, 71.4, 60.6, 58.8, 55.6, 55.4, 30.6, 29.5. IR (KBr, cm^{-1}): 2934, 1714, 1677, 1598, 1514, 1247; ESI-HRMS: calcd for $C_{17}H_{19}N_2O_4$ 315.1345 $[M+H]^+$, found 315.1342.

4-(4-Methoxybenzoyl)hexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4i).



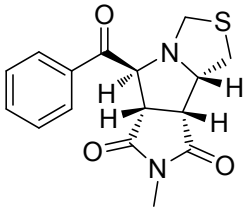
White solid; 159 mg (78%); mp: 118−120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.02 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.82 (d, *J* = 4.7 Hz, 1H), 4.21 (d, *J* = 9.9 Hz, 1H), 3.98 (dd, *J* = 14.5, 6.3 Hz, 1H), 3.89 (d, *J* = 9.9 Hz, 1H), 3.85–3.76 (m, 4H), 3.66 (t, *J* = 8.8 Hz, 1H), 3.07 (dd, *J* = 11.5, 6.6 Hz, 1H), 2.96 (dd, *J* = 11.5, 5.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3, 177.8, 176.2, 164.4, 131.6, 128.1, 114.2, 69.7, 67.0, 57.6, 55.6, 50.9, 49.5, 33.2; IR (KBr, cm^{-1}): 3180, 2933, 1717, 1674, 1597, 1511, 1242. HRMS (ESI, Orbitrap): calcd for $C_{16}H_{17}N_2O_4S$ 333.0909 $[M+H]^+$, found 333.0890.

4-Benzoyl-2-methylhexahydropyrrolo[3,4-*a*]pyrrolizine-1,3(2*H*,4*H*)-dione (4j).



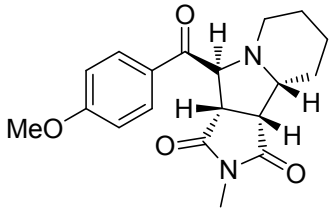
White solid; 119 mg (70%); mp: 95−97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.3 Hz, 2H), 7.73–7.54 (m, 1H), 7.51–7.45 (m, 2H), 5.15 (s, 1H), 3.92 (d, *J* = 8.2 Hz, 1H), 3.87–3.70 (m, 1H), 3.54–3.28 (m, 2H), 2.98 (s, 3H), 2.53–2.46 (m, 1H), 2.33–2.19 (m, 1H), 2.05 (dt, *J* = 14.7, 8.0 Hz, 1H), 1.83 (d, *J* = 7.4 Hz, 1H), 1.68–1.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 179.6, 177.9, 134.7, 133.5, 129.1, 128.7, 70.7, 66.6, 54.1, 49.7, 49.4, 25.9, 25.3, 24.6; IR (KBr, cm^{-1}): 2926, 2815, 1771, 1695, 1596, 1438, 1382, 1284; ESI-HRMS: calcd for $C_{17}H_{19}N_2O_3$ 299.1396 $[M+H]^+$, found 299.1390.

5-Benzoyl-7-methyltetrahydro-3*H*-pyrrolo[3',4':3,4]pyrrolo[1,2-*c*]thiazole-6,8(1*H*,7*H*)-dione (4k).



White solid; 151 mg (78%); mp: 186−187 °C; ^{1}H NMR (300 MHz, $CDCl_3$+$DMSOd_6$) δ 8.11 (d, *J* = 7.6 Hz, 2H), 7.70–7.63 (m, 1H), 7.59–7.50 (m, *J* = 5.9 Hz, 2H), 4.92 (d, *J* = 4.2 Hz, 1H), 4.15 (d, *J* = 9.9 Hz, 1H), 3.99 (dd, *J* = 16.7, 8.2 Hz, 2H), 3.82 (dd, *J* = 8.7, 4.3 Hz, 1H), 3.67 (d, *J* = 3.2 Hz, 1H), 2.99 (dd, *J* = 13.8, 8.0 Hz, 2H), 2.88 (s, 3H). ^{13}C NMR (75 MHz, DMSOd6) δ 195.6, 177.0, 175.7, 134.9, 133.4, 128.8, 128.5, 68.7, 67.9, 57.2, 49.1, 47.9, 32.9, 24.6; IR (KBr, cm^{-1}): 2937, 1771, 1698, 1673, 1430, 1285, 1225; ESI-HRMS: calcd for $C_{16}H_{17}N_2O_3S$ 317.0960 $[M+H]^+$, found 317.0964.

4-(4-Methoxybenzoyl)-2-methyloctahydro-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4l).

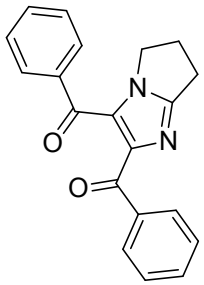


White solid; 120 mg (65%); mp:135−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 5.04 (s, 1H), 3.82 (s, 3H), 3.39–3.12 (m, 3H), 2.95 (s, 3H),

2.80 (d, J = 10.6 Hz, 1H), 2.35 (td, J = 11.4, 2.8 Hz, 1H), 1.94 (d, J = 12.3 Hz, 1H), 1.69 (d, J = 12.9 Hz, 1H), 1.43 (d, J = 12.8 Hz, 1H), 1.32–0.89 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 178.9, 176.9, 164.1, 130.9, 129.4, 114.1, 65.9, 60.4, 55.6, 48.6, 48.1, 47.9, 29.2, 25.4, 25.1, 24.0. IR (KBr, cm^{-1}): 2943, 2852, 1774, 1696, 1599, 1570, 1509, 1436, 1384, 1263; ESI-HRMS: calcd for $C_{19}H_{23}N_2O_4$ 343.1658 $[M+H]^+$, found 343.1644.

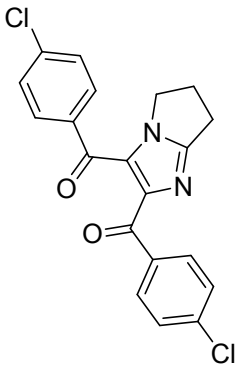
Typical experimental procedure for the synthesis of 6,7-dihydro-5H-pyrrolo[1,2-a]imidazole 5a. To a 25 mL round bottom flask, phenacyl azide **1a** (2.1 mmol), L-proline **2a** (1 mmol), toluene (10 mL) were added and the reaction mixture was refluxed in air for 12 h. Next the toluene was evaporated to yield a crude reaction product which was purified using silica-gel column chromatography to yield **3a** (221 mg, 70%). Using the same protocol, compounds **5b-f** were also synthesized.

(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-diyl)bis(phenylmethanone) (5a).



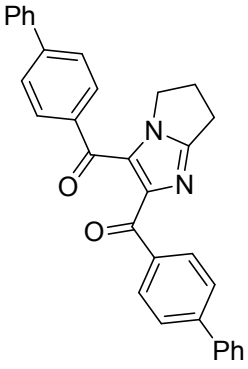
Yellow solid; 221 mg (90% yield); mp: 160−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.4 Hz, 2H), 7.64 (d, J = 7.5 Hz, 2H), 7.52–7.39 (m, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.26 (dd, J = 9.2, 5.6 Hz, 2H), 4.31 (t, J = 7.2 Hz, 2H), 3.03 (t, J = 7.6 Hz, 2H), 2.85–2.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1, 186.9, 156.8, 148.6, 138.2, 137.6, 132.9, 132.7, 129.9, 129.7, 128.9, 128.4, 128.2, 45.8, 26.2, 23.3; IR (KBr, cm^{-1}): 2959, 1640, 1596, 1574, 1504, 1480, 1339, 1221; ESI-HRMS: calcd for $C_{20}H_{17}N_2O_2$ 317.12900 $[M+H]^+$, found 317.12914.

(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-diyl)bis((4-chlorophenyl)methanone) (5b).



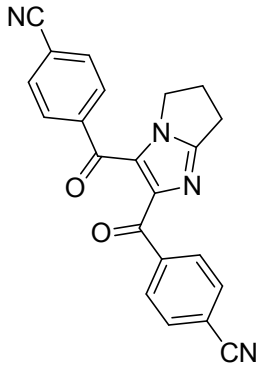
Pale yellow solid; 250 mg (85%); mp: 180−181 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.29 (t, *J* = 7.2 Hz, 2H), 3.02 (t, *J* = 7.6 Hz, 2H), 2.86–2.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 185.6, 156.9, 148.0, 139.5, 139.4, 136.3, 135.6, 131.6, 130.2, 129.8, 128.8, 128.6, 45.8, 26.1, 23.3; IR (KBr, cm^{-1}): 2927, 2854, 1653, 1630, 1583, 1374, 1214; ESI-HRMS: calcd for $C_{20}H_{15}Cl_2N_2O_2$ 385.05106 $[M+H]^+$, found 385.05227.

(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-diyl)bis([1,1'-biphenyl]-4-ylmethanone) (5c).



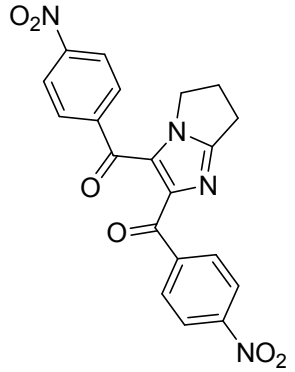
Pale yellow solid ; 285 mg (81%); mp: 210−211 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.58-7.53 (m, 6H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.48–7.35 (m, 6H), 4.33 (t, *J* = 7.2 Hz, 2H), 3.06 (t, *J* = 7.6 Hz, 2H), 2.84 –2.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 186.5, 156.8, 148.5, 145.6, 145.4, 140.1, 139.8, 136.9, 136.5, 130.7, 130.0, 129.6, 128.9, 128.8, 128.2, 128.1, 127.3, 127.0, 126.9, 45.8, 26.2, 23.4; IR (KBr, cm^{-1}): 2926, 1637, 1600, 1506, 1482, 1339, 1225; ESI-HRMS: calcd for $C_{32}H_{25}N_2O_2$ 469.19160 $[M+H]^+$, found 469.19161.

4,4'-(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-dicarbonyl)dibenzonitrile (5d).



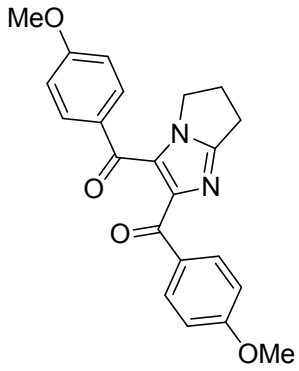
Pale yellow solid; 220 mg (80%); mp: 159−160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 4.32 (t, *J* = 7.0 Hz, 2H), 3.05 (t, *J* = 7.5 Hz, 2H), 2.84–2.69 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.5, 185.4, 157.5, 147.6, 141.1, 140.0, 132.5, 132.3, 132.1, 130.8, 130.1, 129.1, 118.1, 117.8, 116.2, 46.0, 26.1, 23.3; IR (KBr, cm^{-1}): 2925, 2229, 1644, 1603, 1506, 1336, 1221. ESI-HRMS: calcd for $C_{22}H_{15}N_4O_2$ 367.11950 $[M+H]^+$, 367.11950, found 367.12051.

(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-diyl)bis((4-nitrophenyl)methanone) (5e).



Red solid; 235 mg (78%); mp: 240-241 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.6 Hz, 2H), 8.25 (d, *J* = 8.6 Hz, 2H), 8.22 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 2H), 4.35 (t, *J* = 7.1 Hz, 2H), 3.06 (t, *J* = 7.5 Hz, 2H), 2.79 (dd, *J* = 14.6, 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO) δ 191.0, 189.9, 162.5, 154.7, 152.1, 147.6, 146.4, 144.8, 136.3, 134.6, 133.9, 128.4, 128.1, 50.8, 30.8, 28.0; IR (KBr, cm^{-1}): 2924, 2854, 1657, 1639, 1599, 1520, 1347, 1218; ESI-HRMS: calcd for $C_{20}H_{15}N_4O_6$ 407.09916 $[M+H]^+$, found 407.09978.

(6,7-Dihydro-5*H*-pyrrolo[1,2-*a*]imidazole-2,3-diyl)bis((4-methoxyphenyl)methanone) (5f).



Brown solid; 226 mg (80%); mp: 175−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 4.7 Hz, 2H), 7.69 (d, *J* = 4.9 Hz, 2H), 6.85 (d, *J* = 6.6 Hz, 2H), 6.76 (d, *J* = 5.7 Hz, 2H), 4.27 (s, 2H), 3.85 (s, 3H), 3.80 (s, 3H), 3.01 (s, 2H), 2.72 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.7, 185.6, 163.5, 163.3, 156.3, 148.2, 133.3, 132.5, 131.4, 130.7, 129.8, 113.7, 113.4, 55.5, 55.4, 45.6, 26.1, 23.3; ESI-HRMS: calcd for $C_{22}H_{21}N_2O_4$ 377.15013 $[M+H]^+$, found 377.15092.

Crystallographic data for BB98 (Compound **4a**)

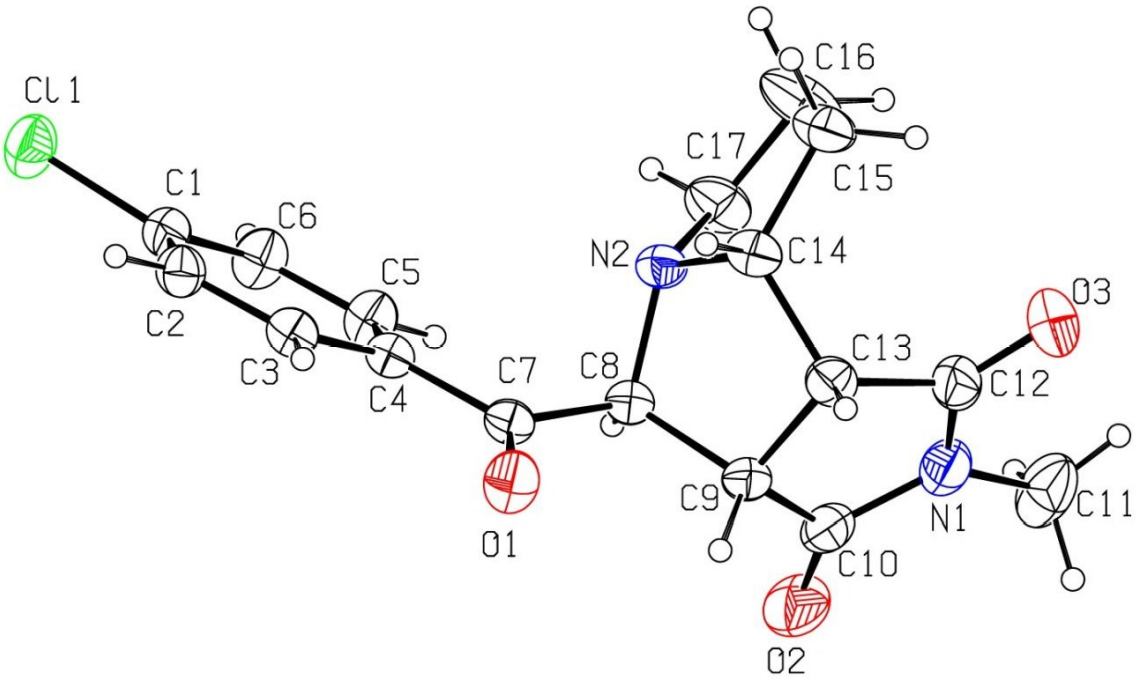
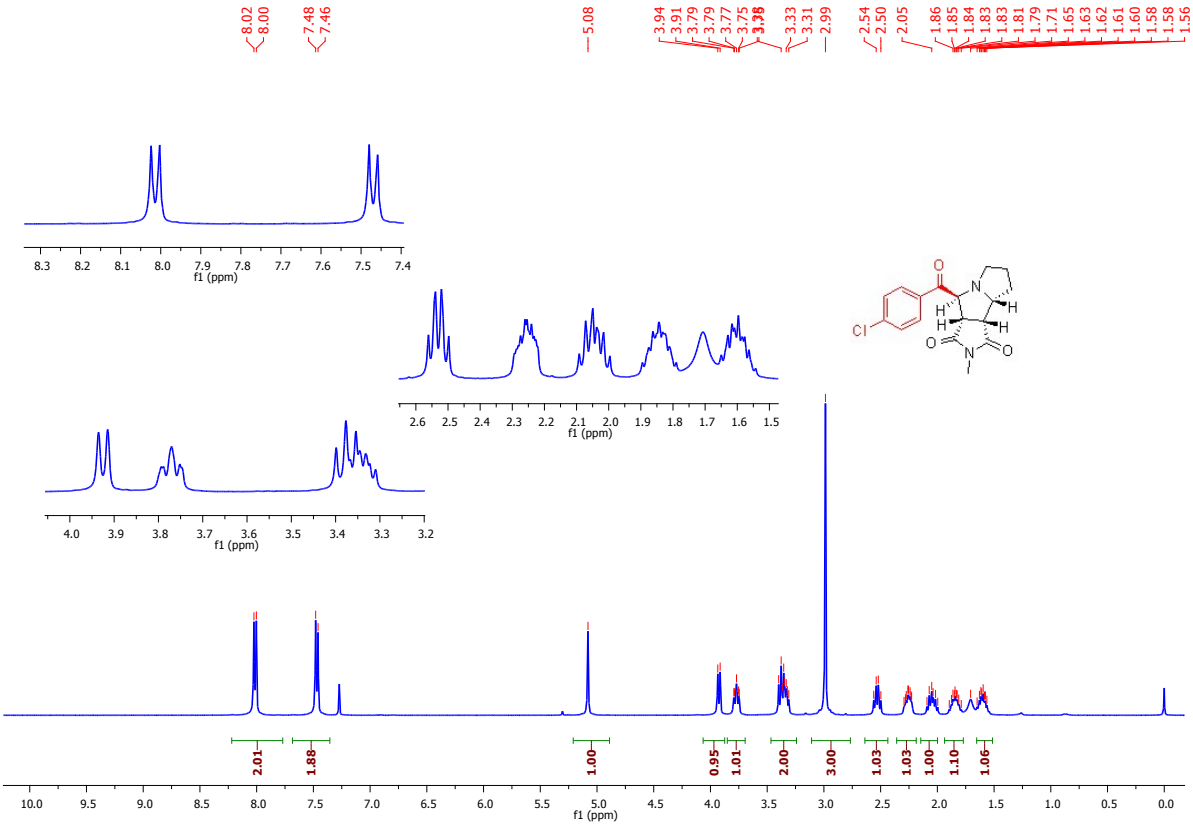


Figure 1. ORTEP diagram of BB98 (Compound **4a**) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius.

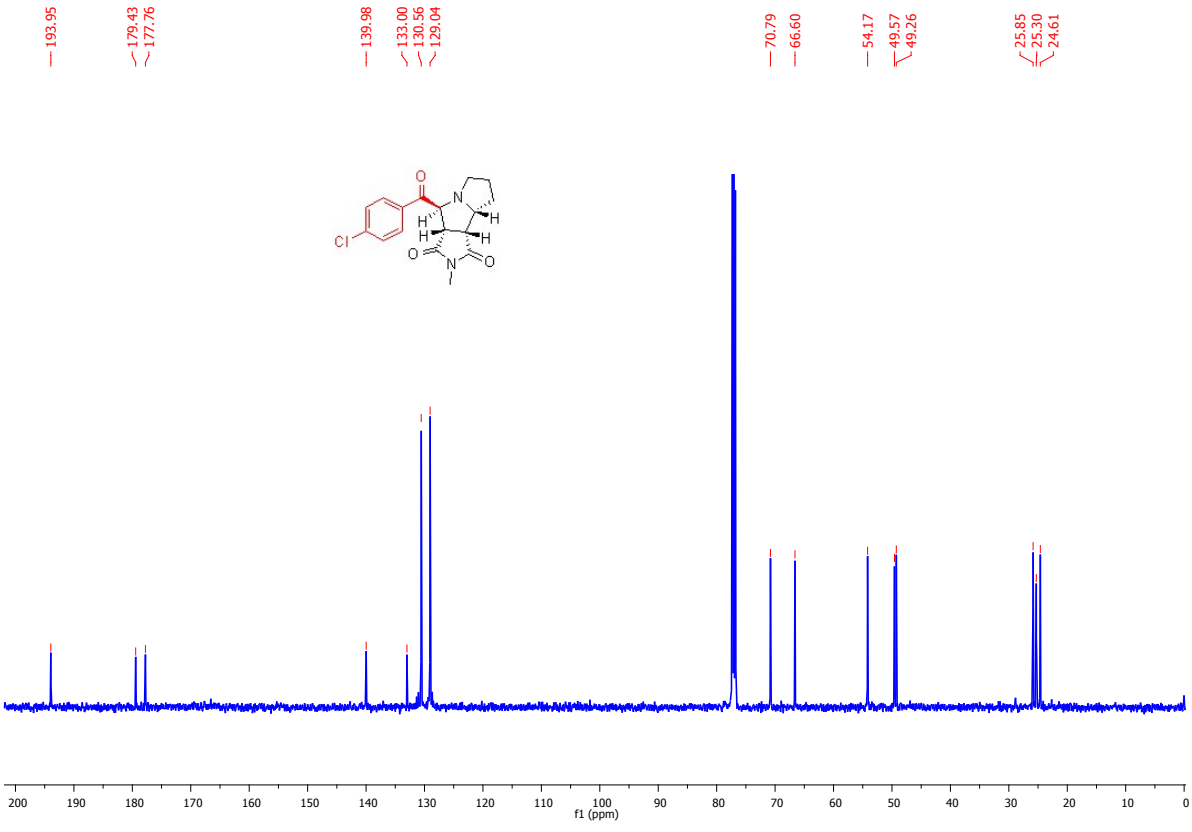
X-ray data for the compound were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated Mo-Kα radiation (λ=0.71073Å) with ω-scan method.1 Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 6242 reflections. Integration and scaling of intensity data were accomplished using SAINT program.1 The structures were solved by Direct Methods using SHELXS972 and refinement was carried out by full-matrix least-squares technique using SHELXL- 2014/7.2 Anisotropic displacement parameters were included for all non-hydrogen atoms. H bound to N atom was located from the difference Fourier map. All H atoms were positioned geometrically and treated as riding on their parent C atoms with C-H distances of 0.93-0.97 Å, and with Uiso(H) = 1.2Ueq (C) or 1.5Ueq for methyl atoms.

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, http://shelx.uni-ac.gwdg.de/SHELX/index.php

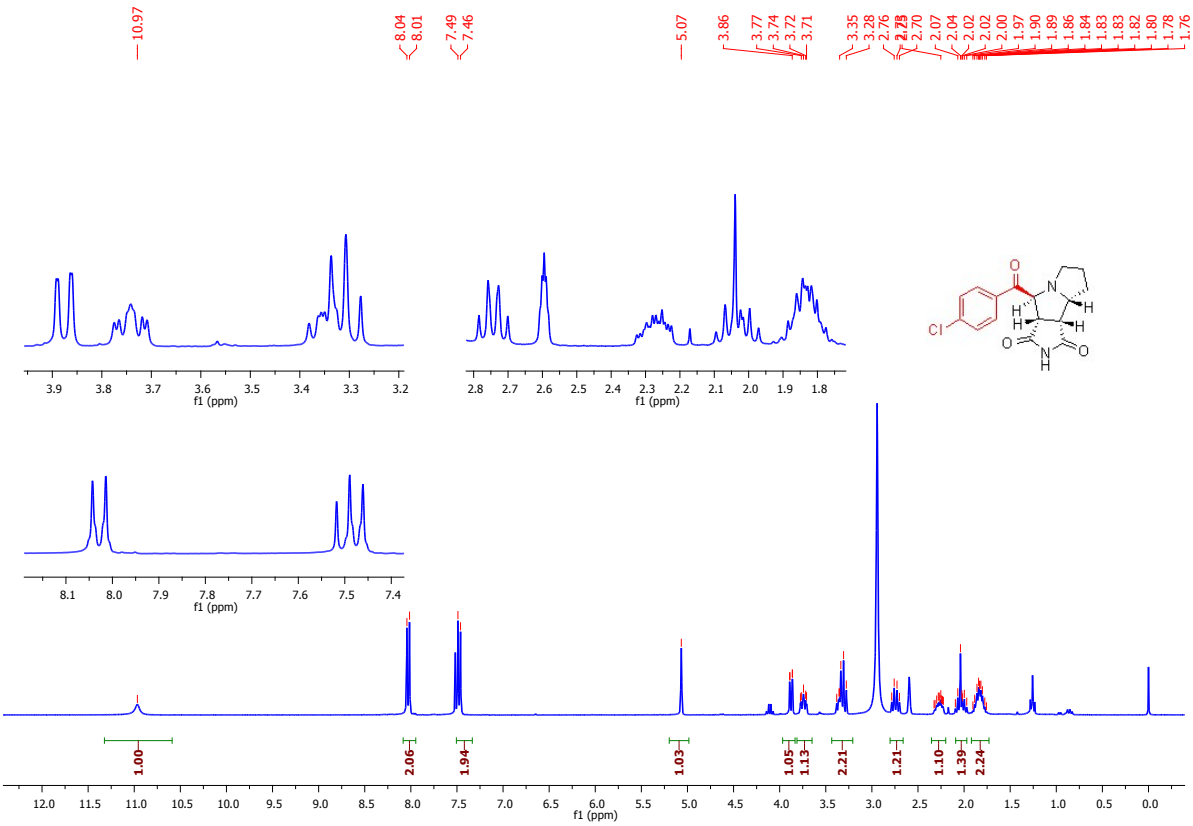
Crystal data for BB98 (Compound 4a): C17H17N2O3Cl, M = 332.77, size 0.28 x 0.24 x 0.19 mm3, monoclinic, space group $P21/n$ (No. 14), a = 12.4653(16), b = 8.3351(11), c = 16.192(2) Å, β = 110.902(2)°, V = 1571.6(3) Å3, Z = 4, Dc = 1.406 g/cm3, F000 = 696, CCD area detector, MoKα radiation, λ = 0.71073Å, T = 293(2)K, 2θmax = 55°, 16635 reflections collected, 3595 unique (Rint = 0.021), Final $GooF$ = 1.04, R1 = 0.0463, wR2 = 0.1368, R indices based on 2940 reflections with $I > 2\sigma(I)$ (refinement on F2), 209 parameters, μ = 0.260 mm−1, Min and Max Resd. Dens. = -0.24 and 0.28 e/Å3. CCDC 1493300 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://summary.ccdc.cam.ac.uk/structure-summary-form or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.



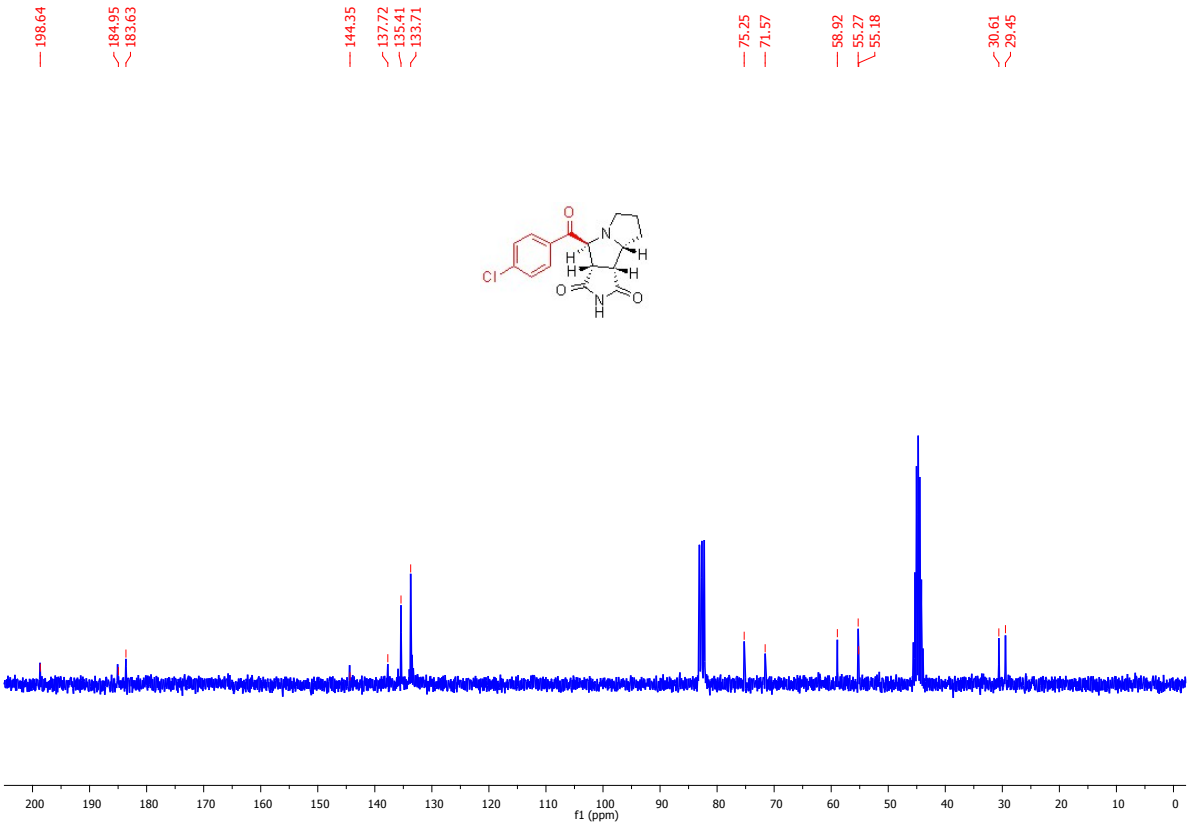
^{1}H NMR spectrum of **4a** (400 MHz, $CDCl_3$)



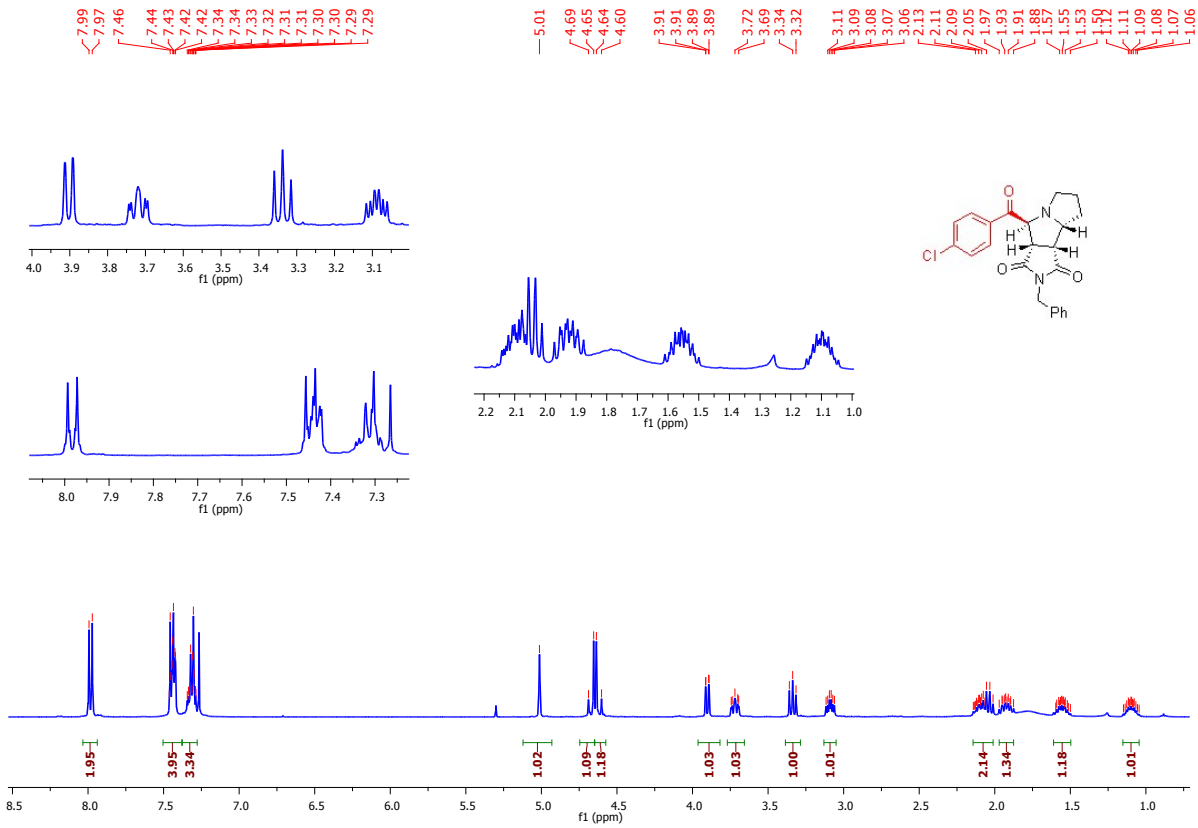
^{13}C NMR spectrum of **4a** (125 MHz, $CDCl_3$)



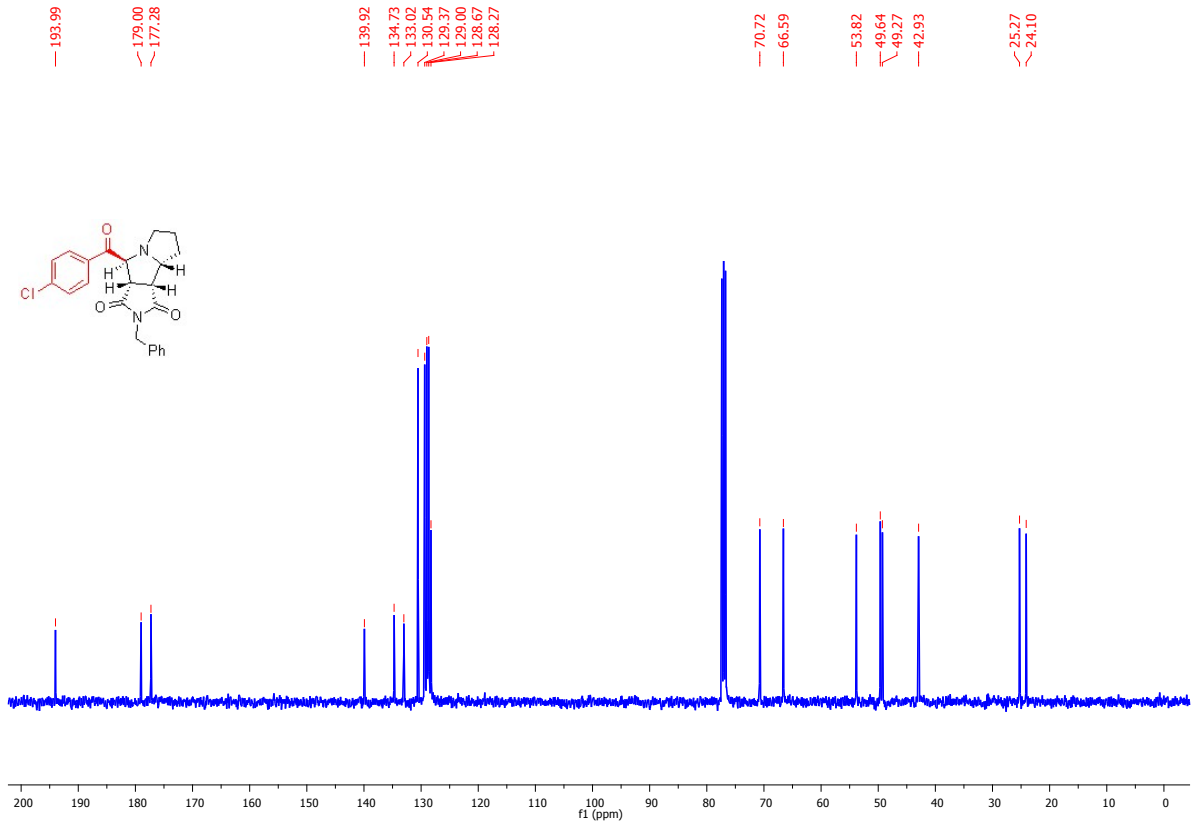
^{1}H NMR spectrum of **4b** (300 MHz, $CDCl_3$+$DMSOd_6$)



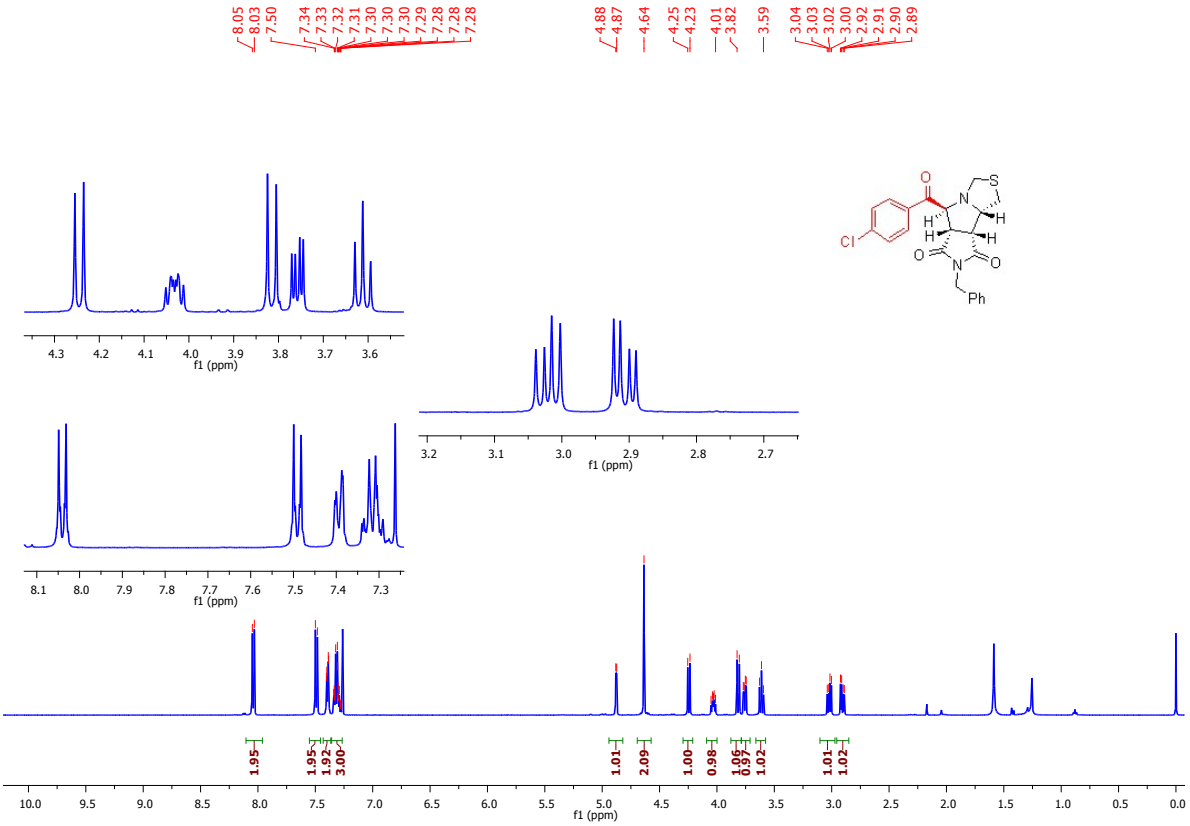
^{13}C NMR spectrum of **4b** (75 MHz, $CDCl_3$+$DMSOd_6$)



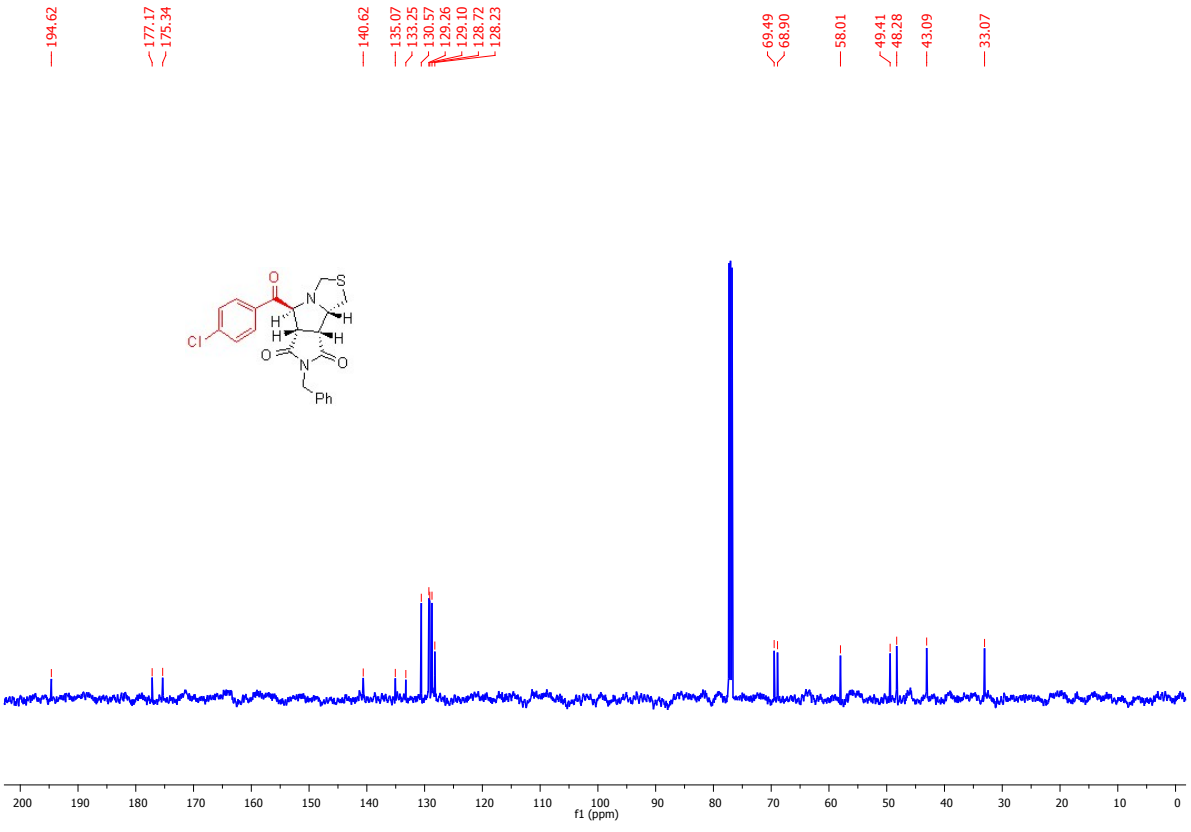
^{1}H NMR spectrum of **4c** (400 MHz, $CDCl_3$)



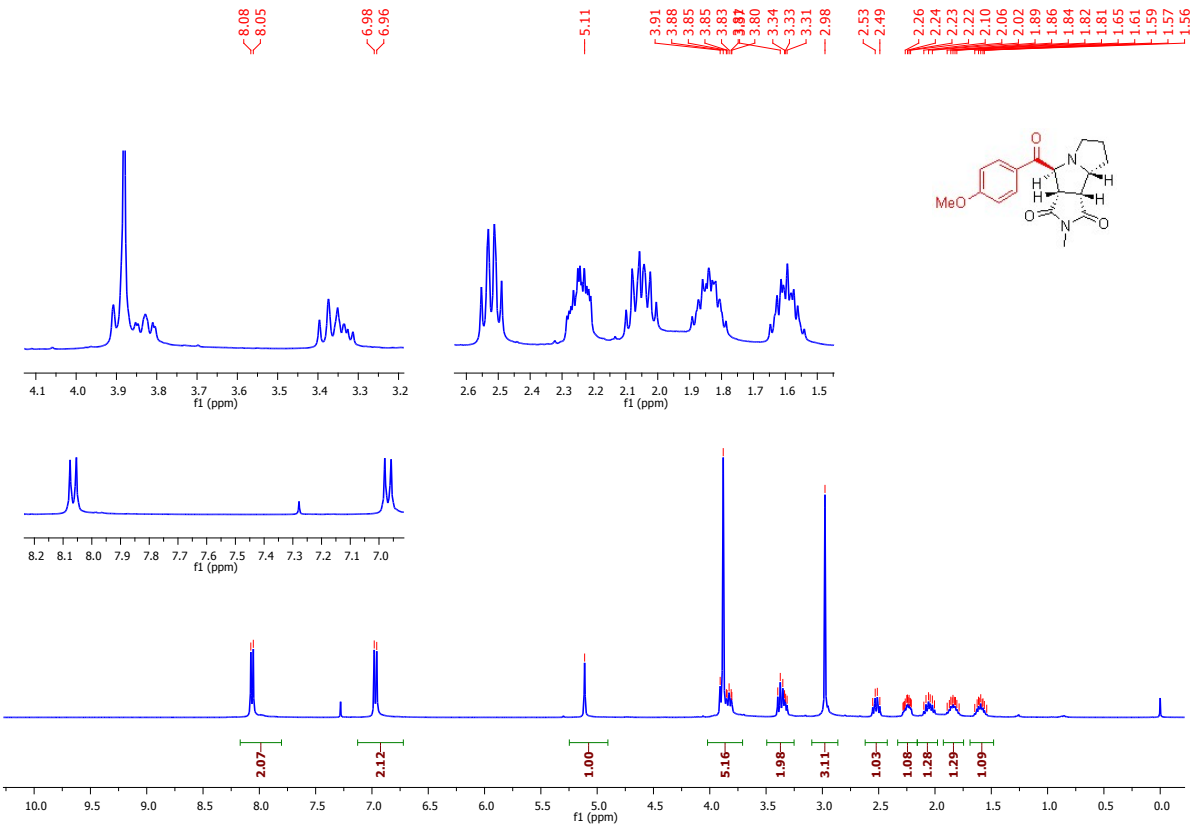
^{13}C NMR spectrum of **4c** (100 MHz, $CDCl_3$)



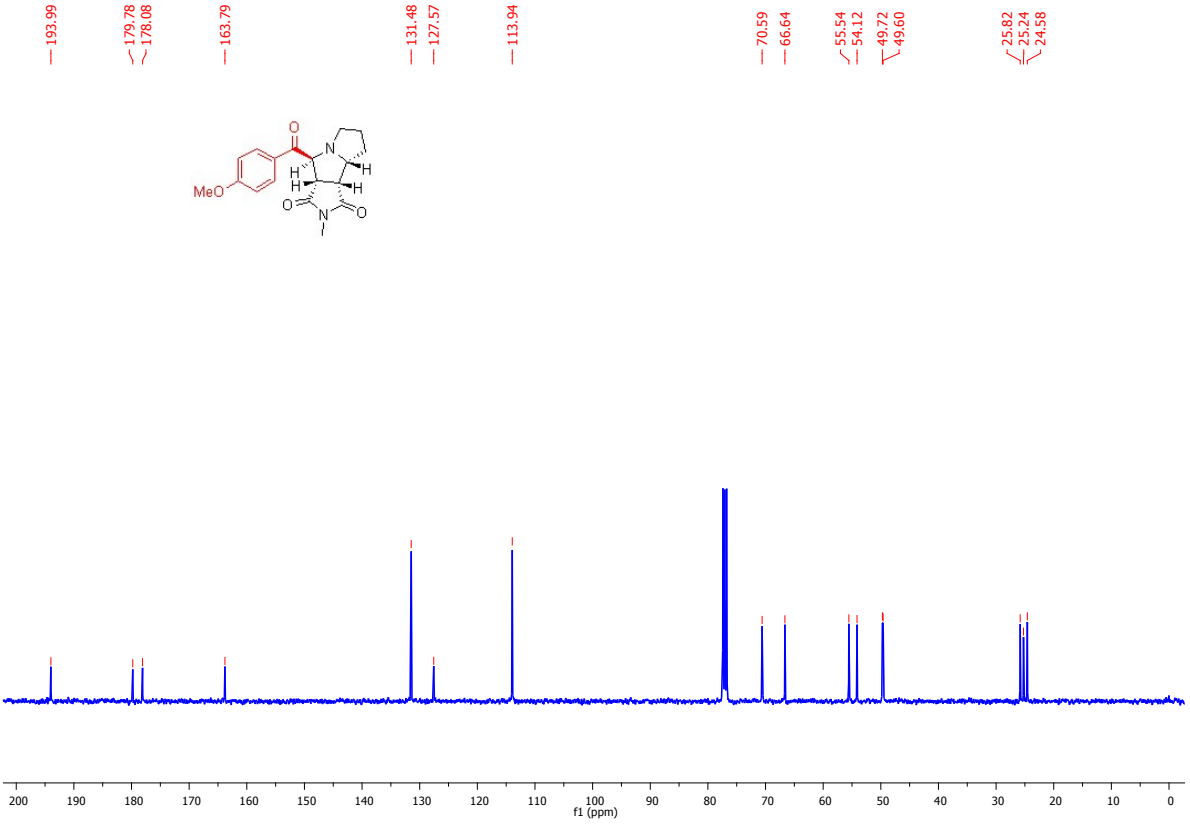
^{1}H NMR spectrum of **4d** (400 MHz, $CDCl_3$)



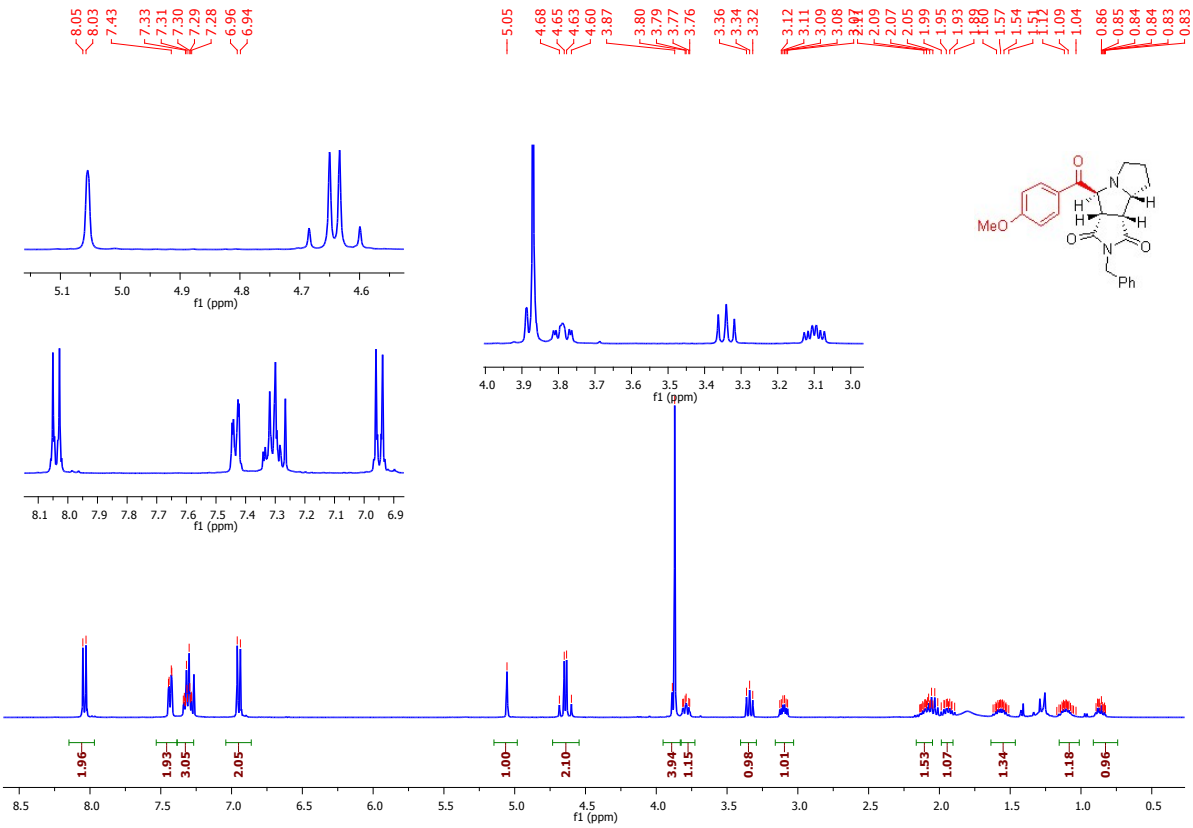
^{13}C NMR spectrum of **4d** (125 MHz, $CDCl_3$)



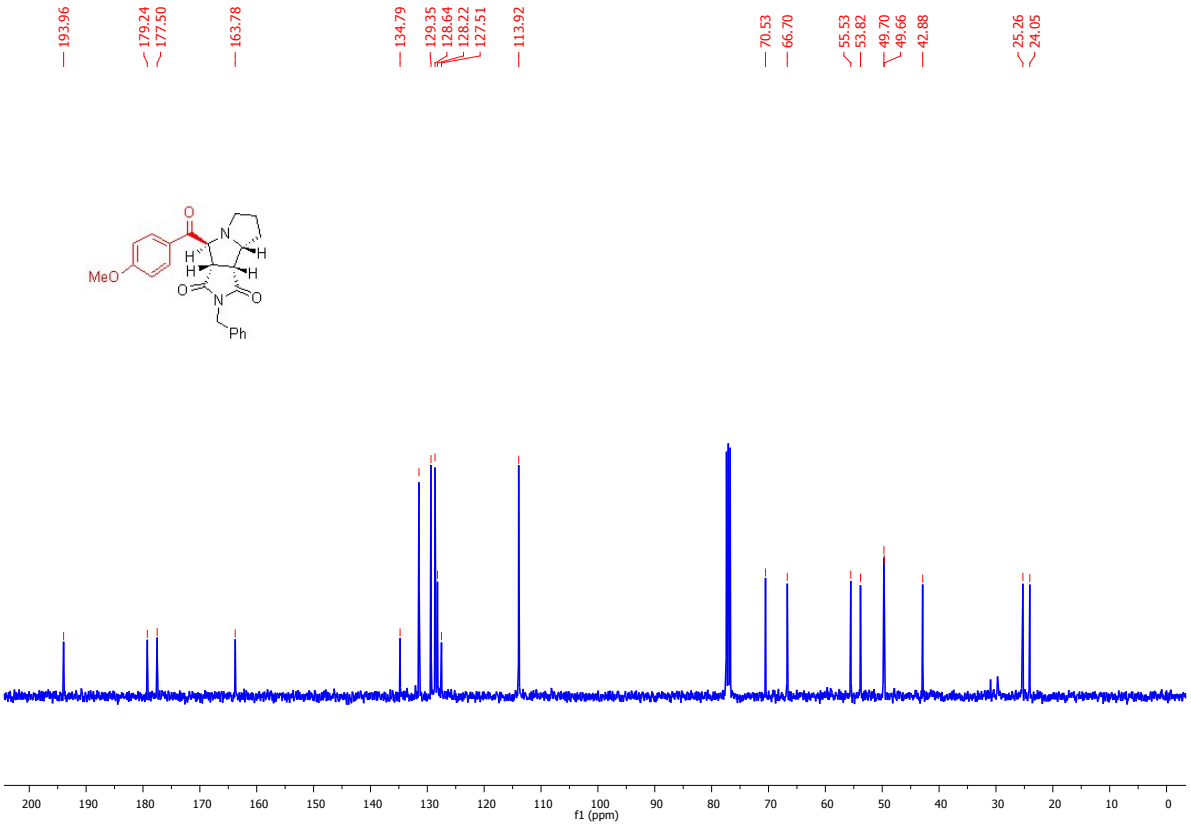
^{1}H NMR spectrum of **4e** (400 MHz, $CDCl_3$)



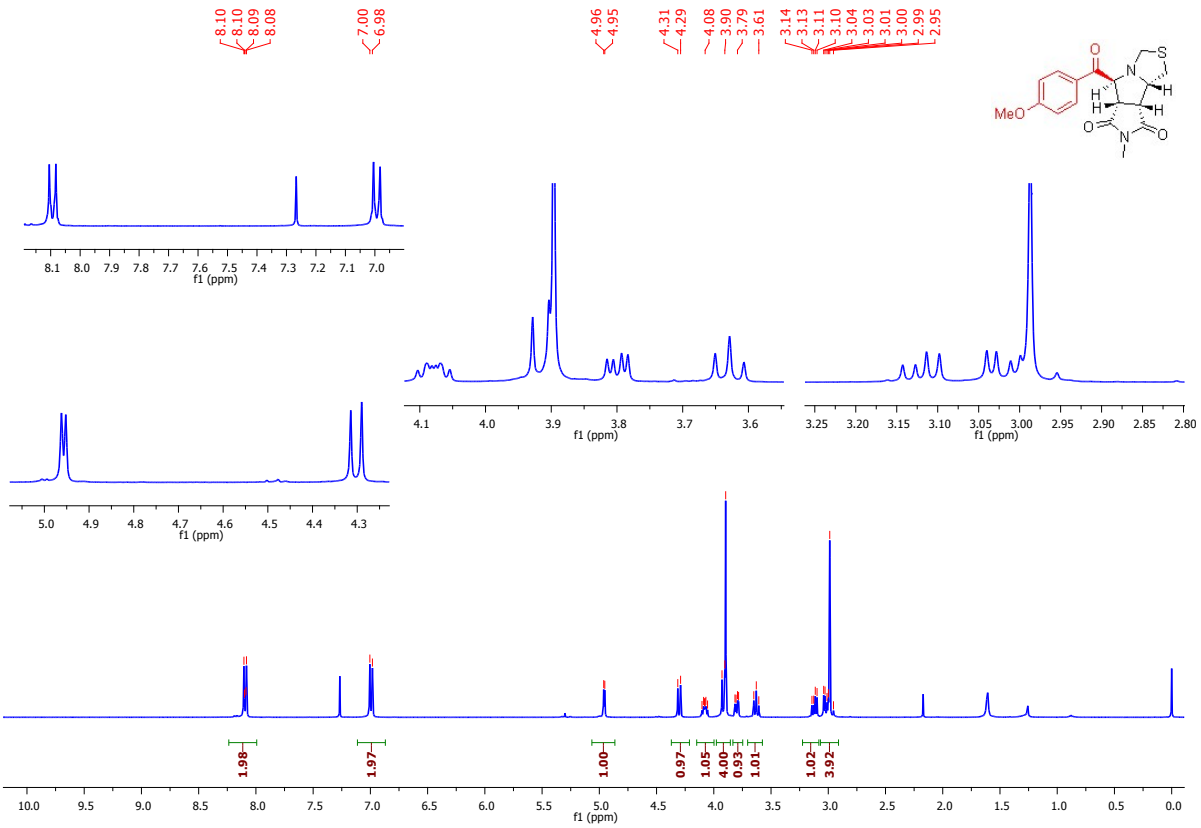
^{13}C NMR spectrum of **4e** (100 MHz, $CDCl_3$)



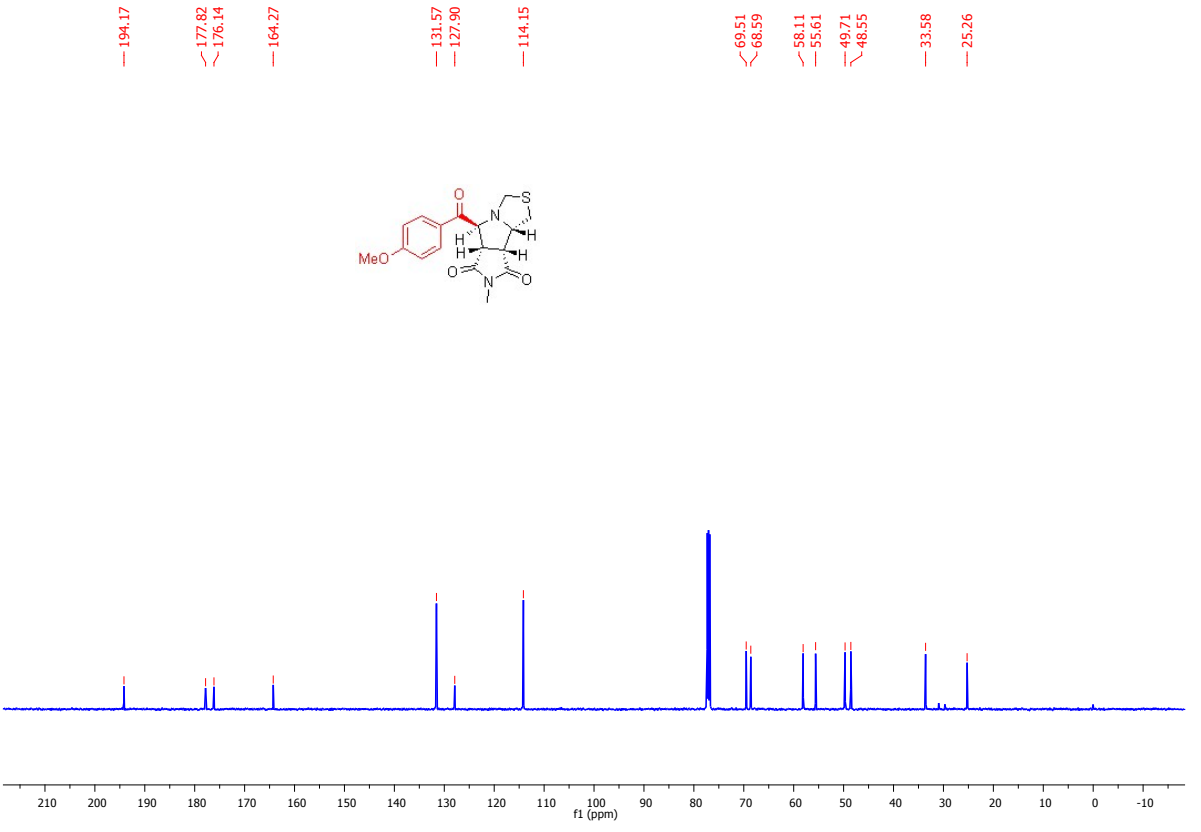
^{1}H NMR spectrum of **4f** (400 MHz, $CDCl_3$)



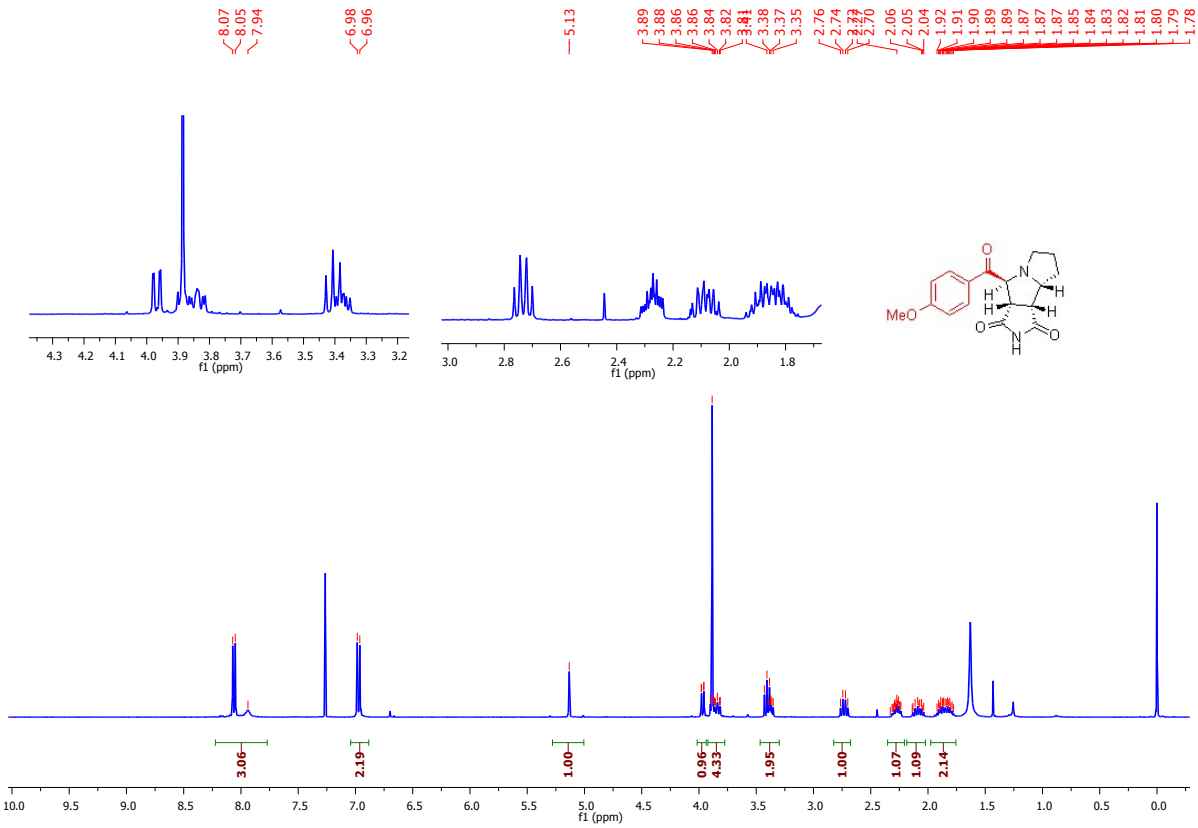
^{13}C NMR spectrum of **4f** (100 MHz, $CDCl_3$)



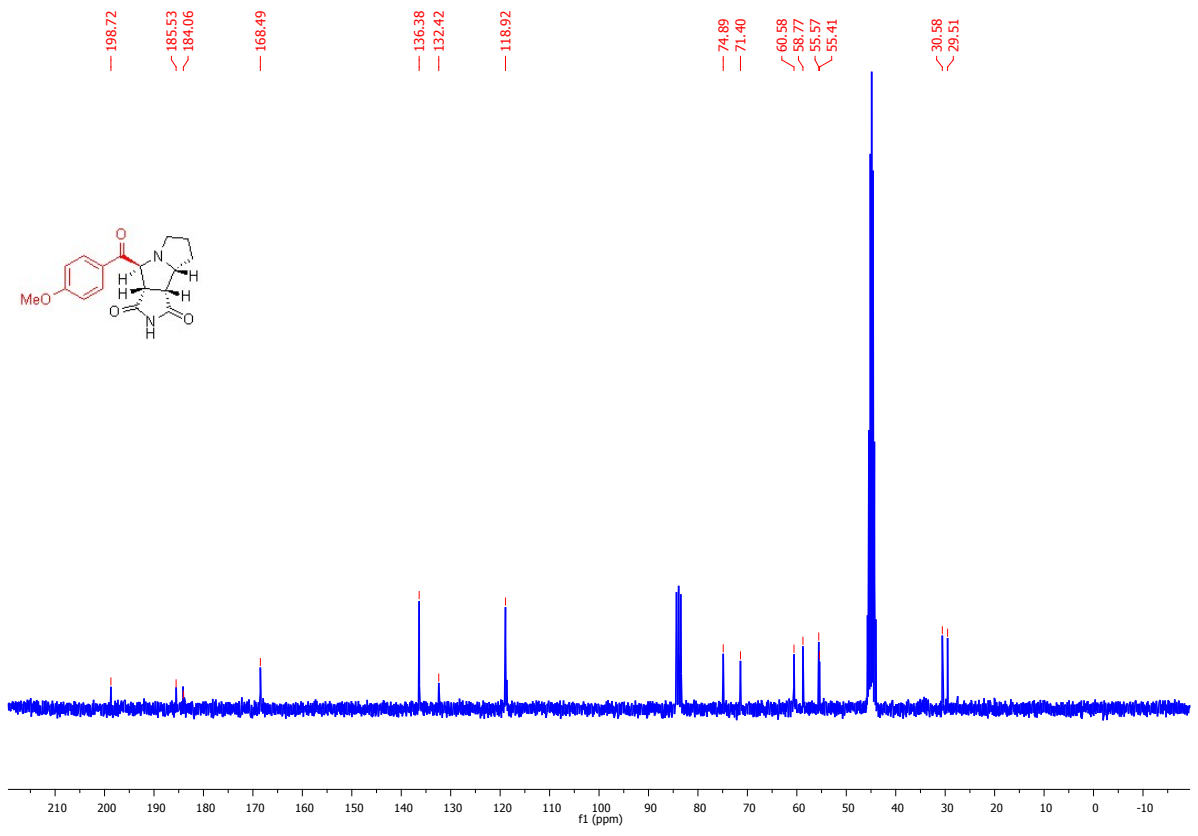
^{1}H NMR spectrum of **4g** (400 MHz, $CDCl_3$)



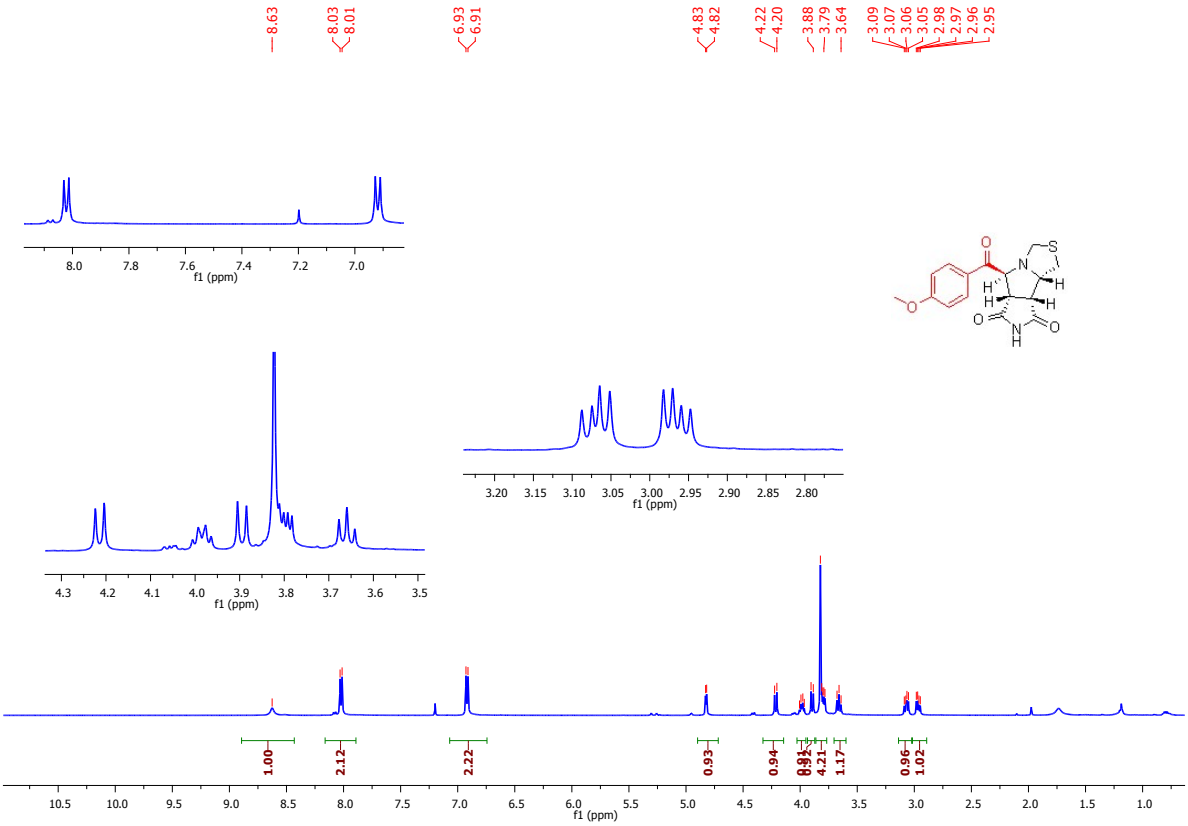
^{13}C NMR spectrum of **4g** (125 MHz, $CDCl_3$)



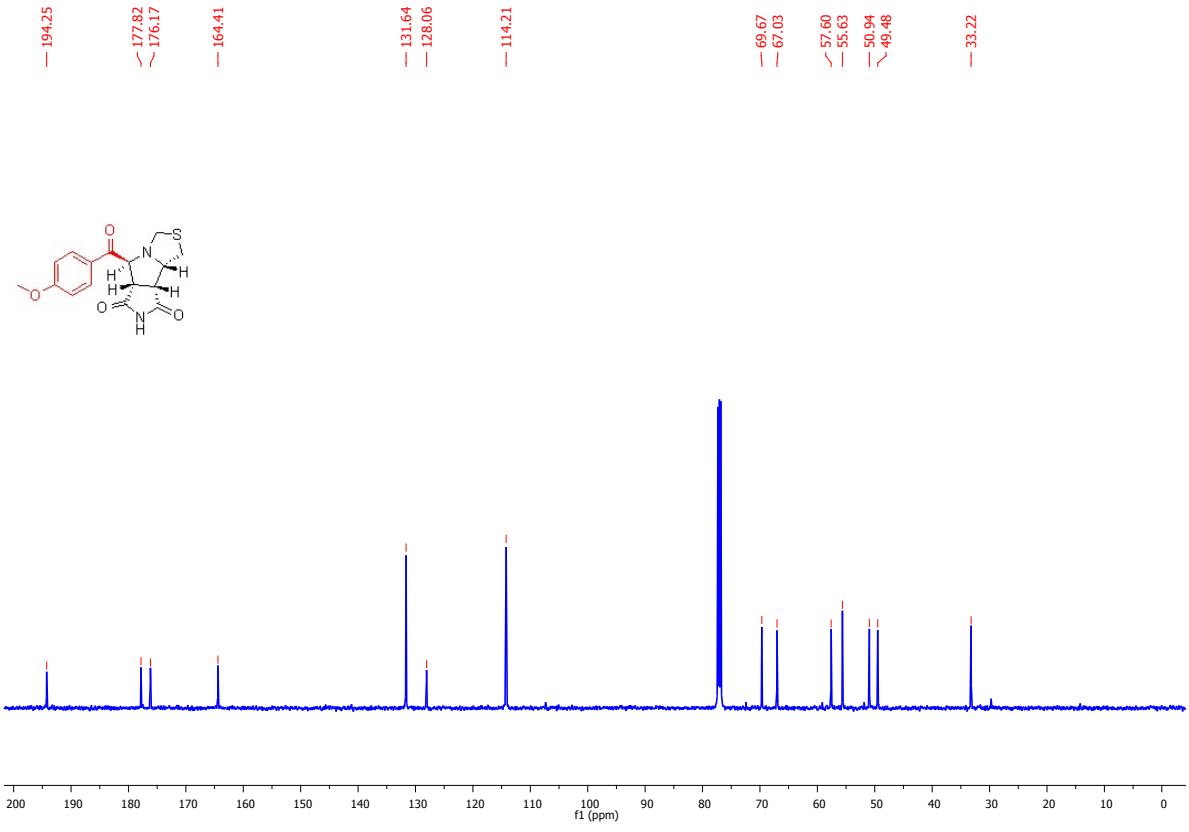
^{1}H NMR spectrum of **4h** (400 MHz, $CDCl_3$)



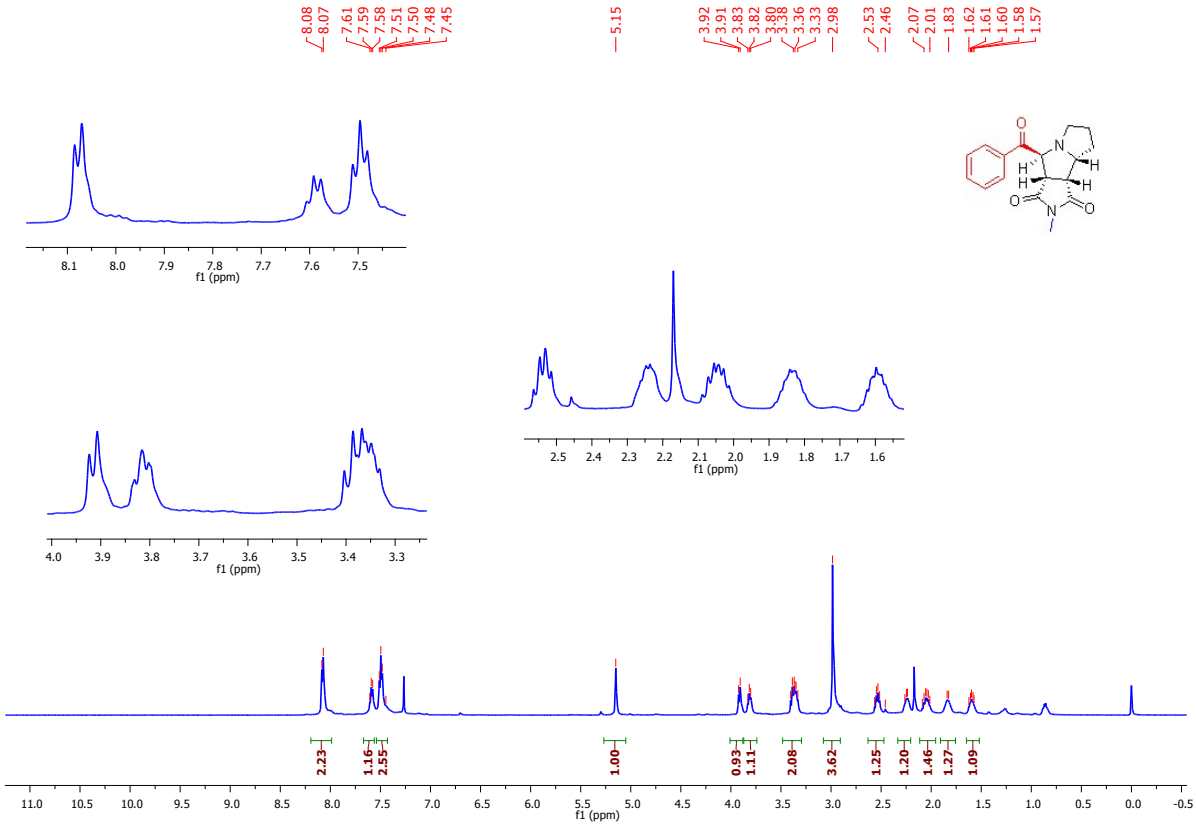
^{13}C NMR spectrum of **4h** (75 MHz, $CDCl_3$+$DMSOd_6$)



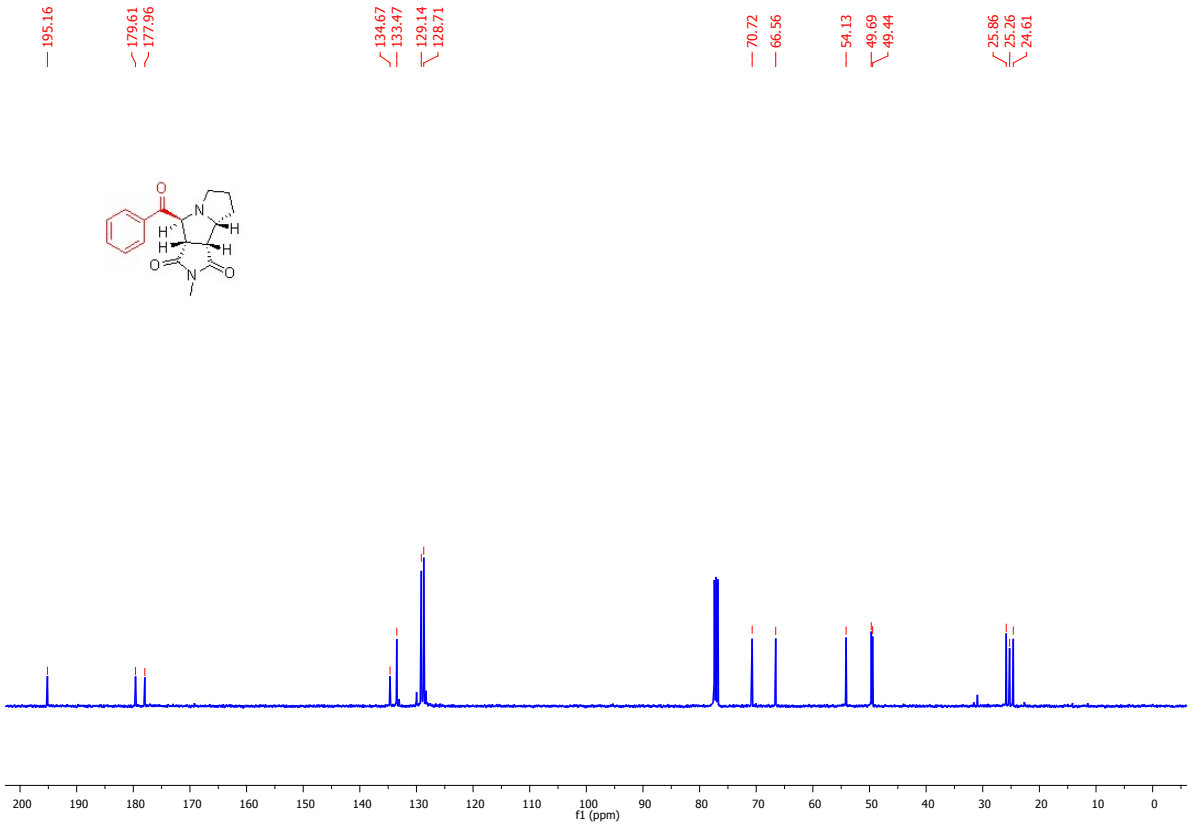
^{1}H NMR spectrum of **4i** (500 MHz, $CDCl_3$)



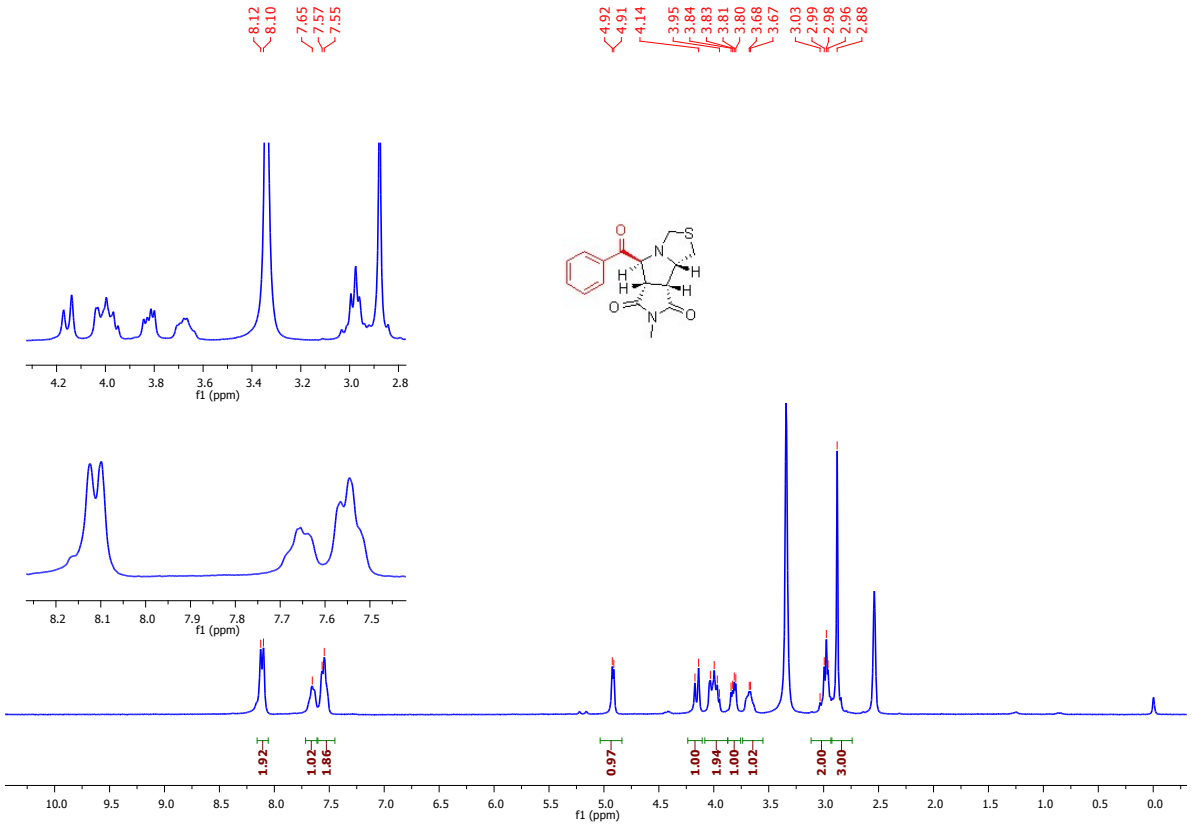
^{13}C NMR spectrum of **4i** (125 MHz, $CDCl_3$)



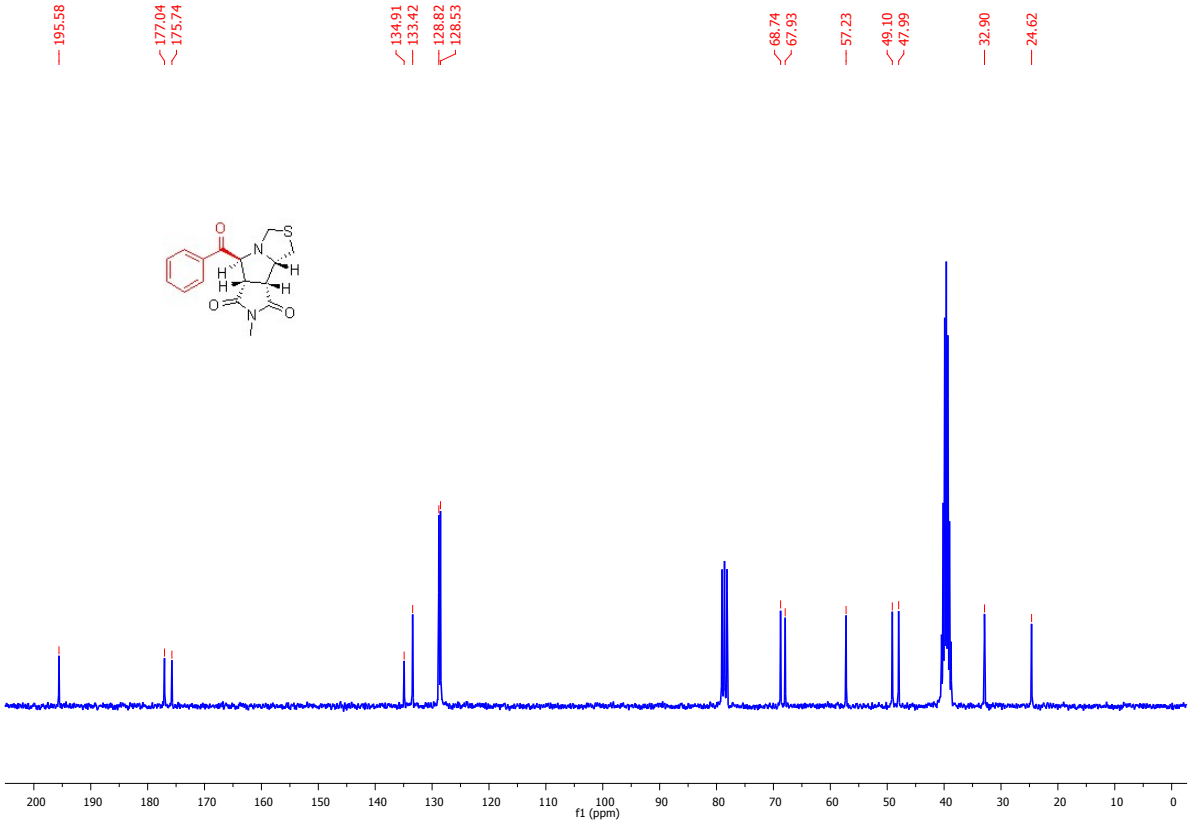
^{1}H NMR spectrum of **4j** (500 MHz, $CDCl_3$)



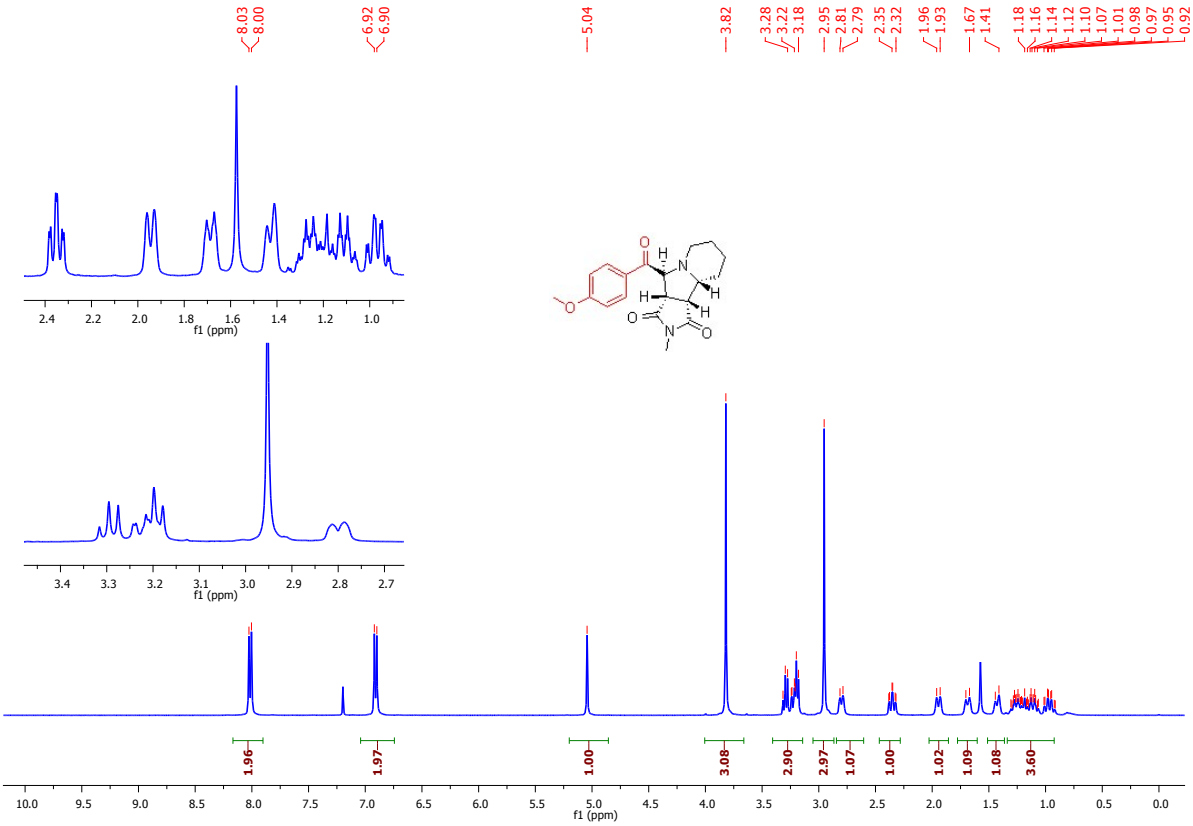
^{13}C NMR spectrum of **4j** (100 MHz, $CDCl_3$)



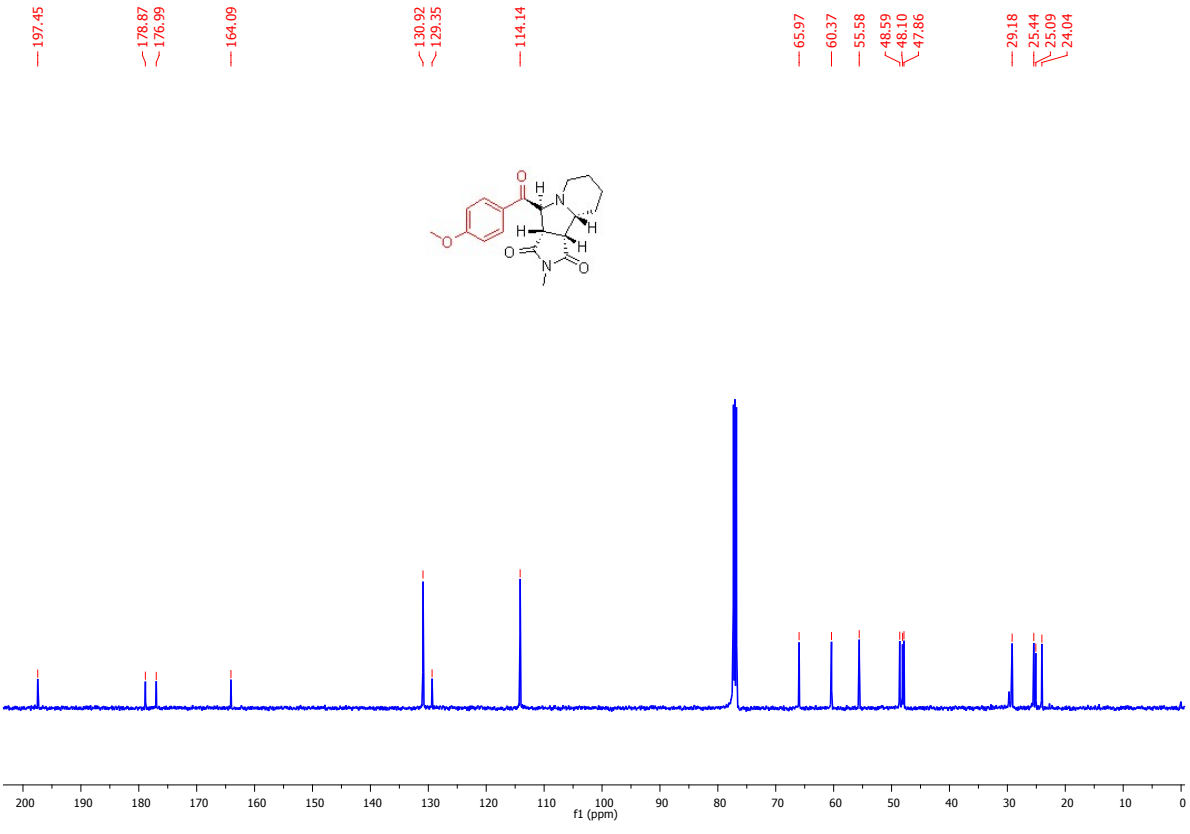
^{1}H NMR spectrum of **4k** (300 MHz, $CDCl_3$+$DMSOd_6$)



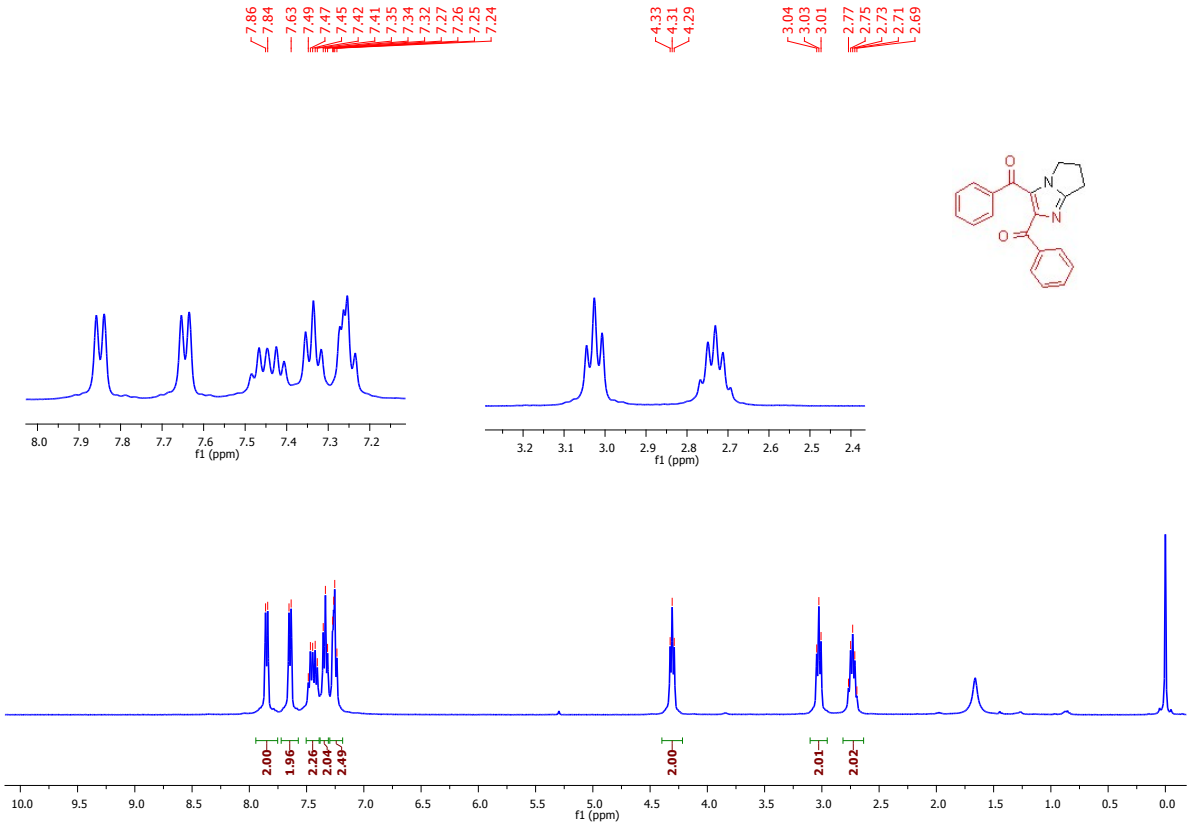
^{13}C NMR spectrum of **4k** (75 MHz, $CDCl_3$+$DMSOd_6$)



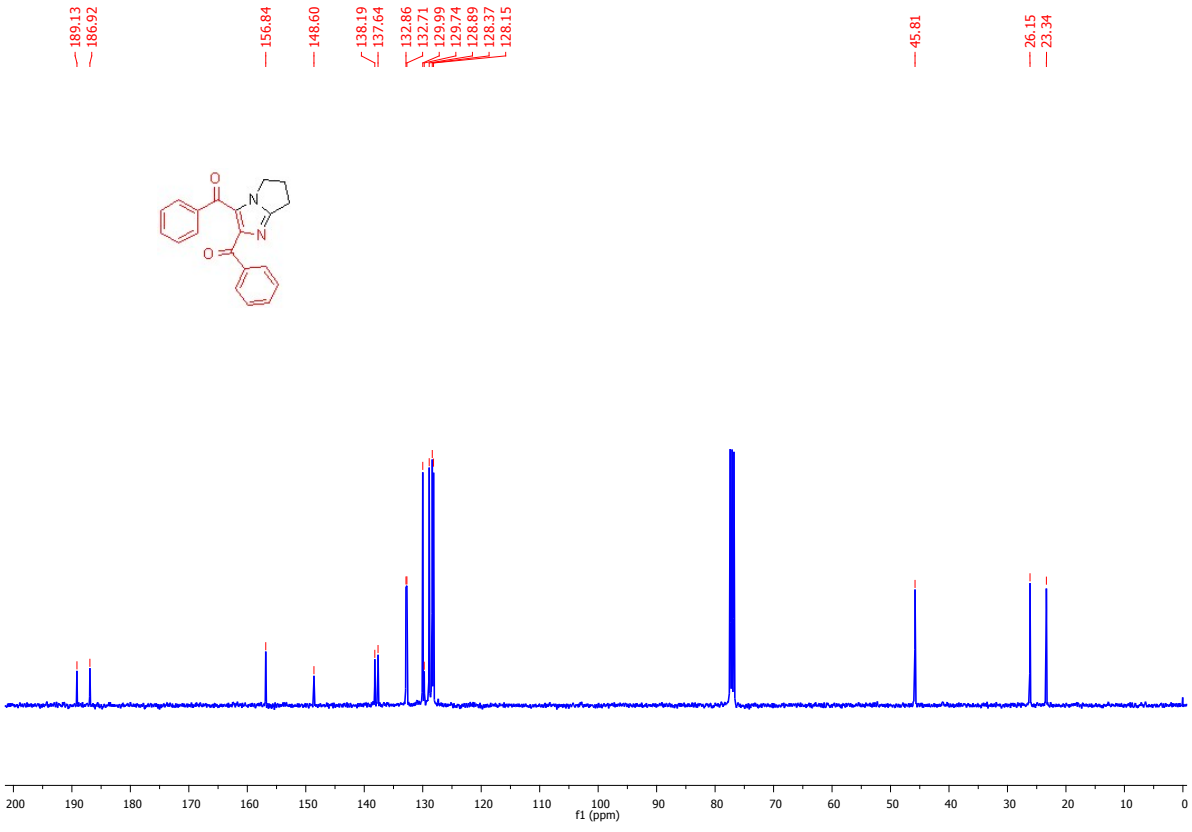
^{1}H NMR spectrum of **4l** (400 MHz, $CDCl_3$)



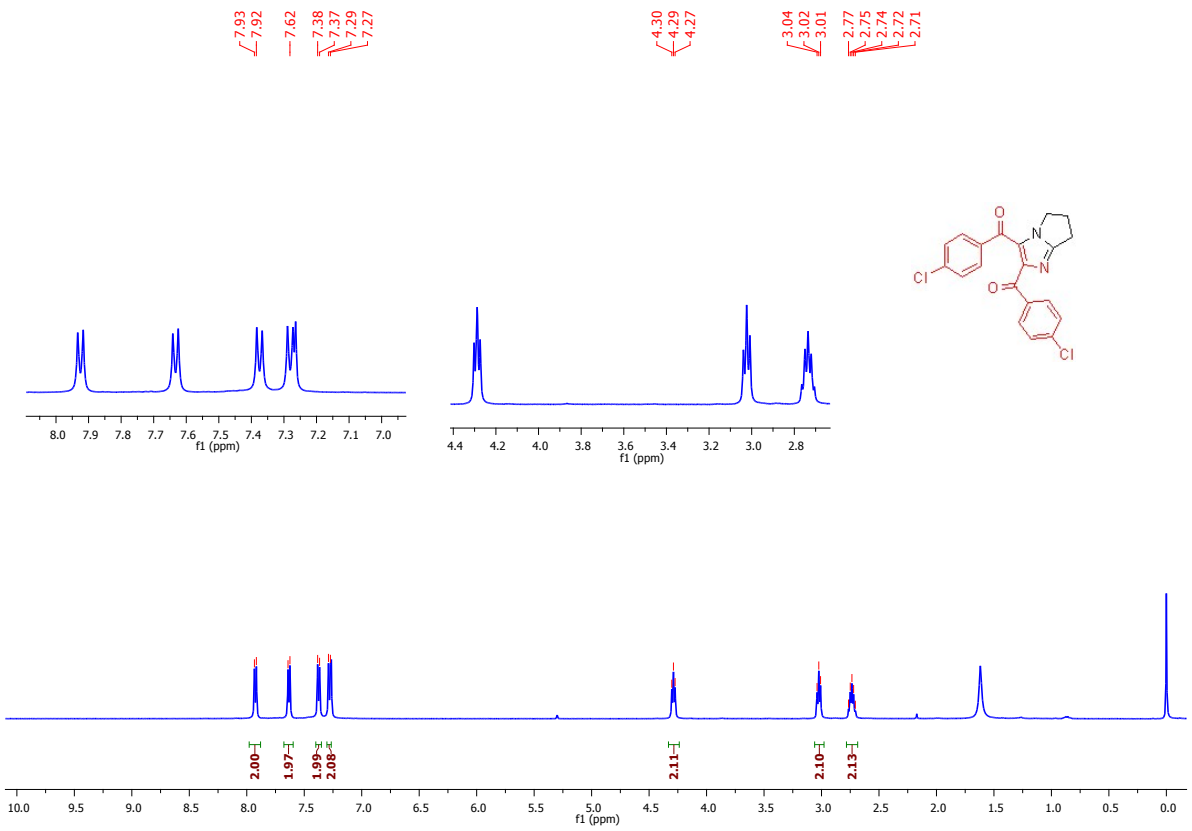
^{13}C NMR spectrum of **4l** (125 MHz, $CDCl_3$)



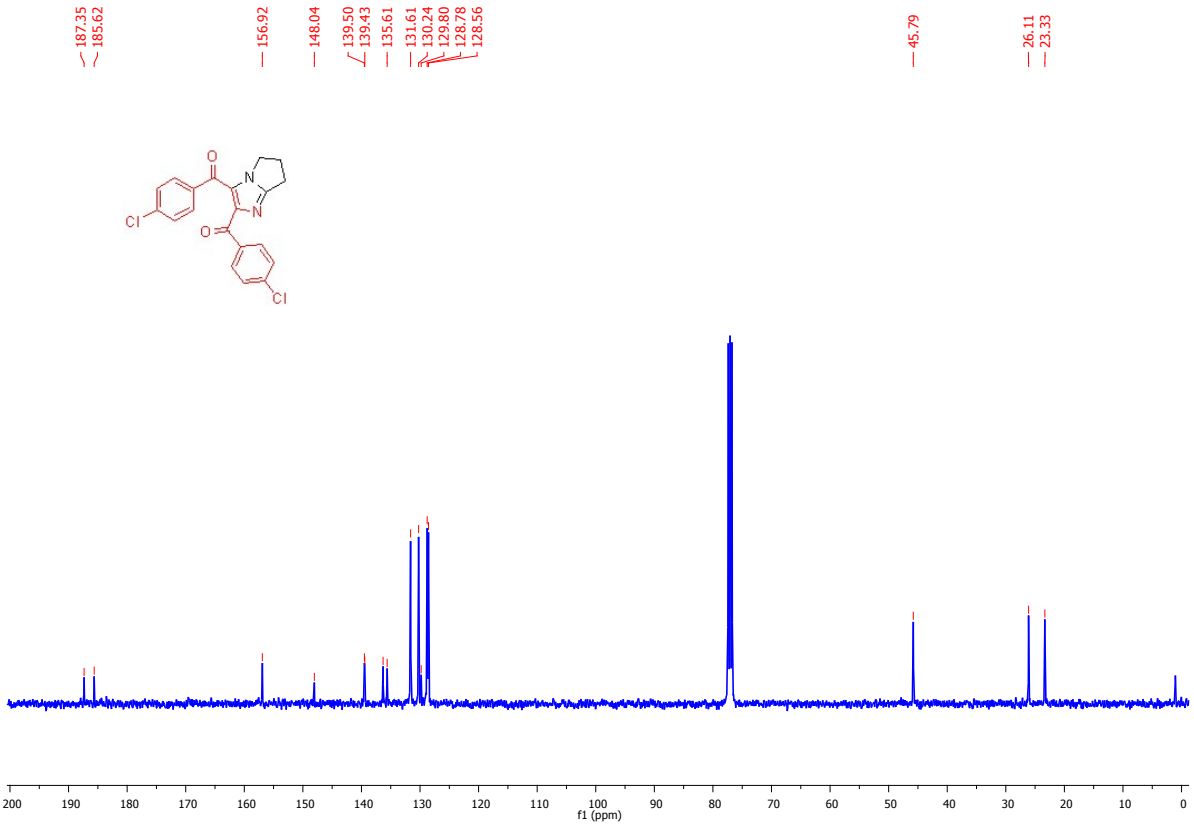
^{1}H NMR spectrum of **5a** (400 MHz, $CDCl_3$)



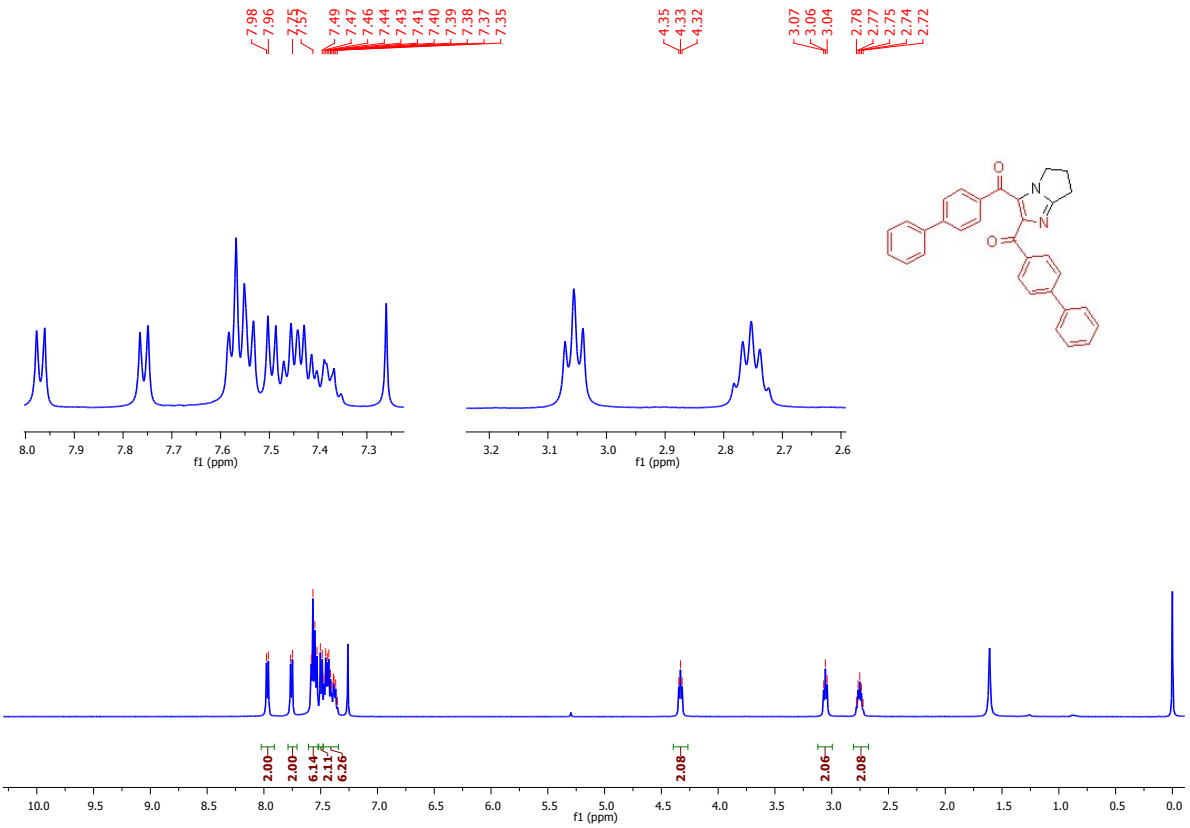
^{13}C NMR spectrum of **5a** (100 MHz, $CDCl_3$)



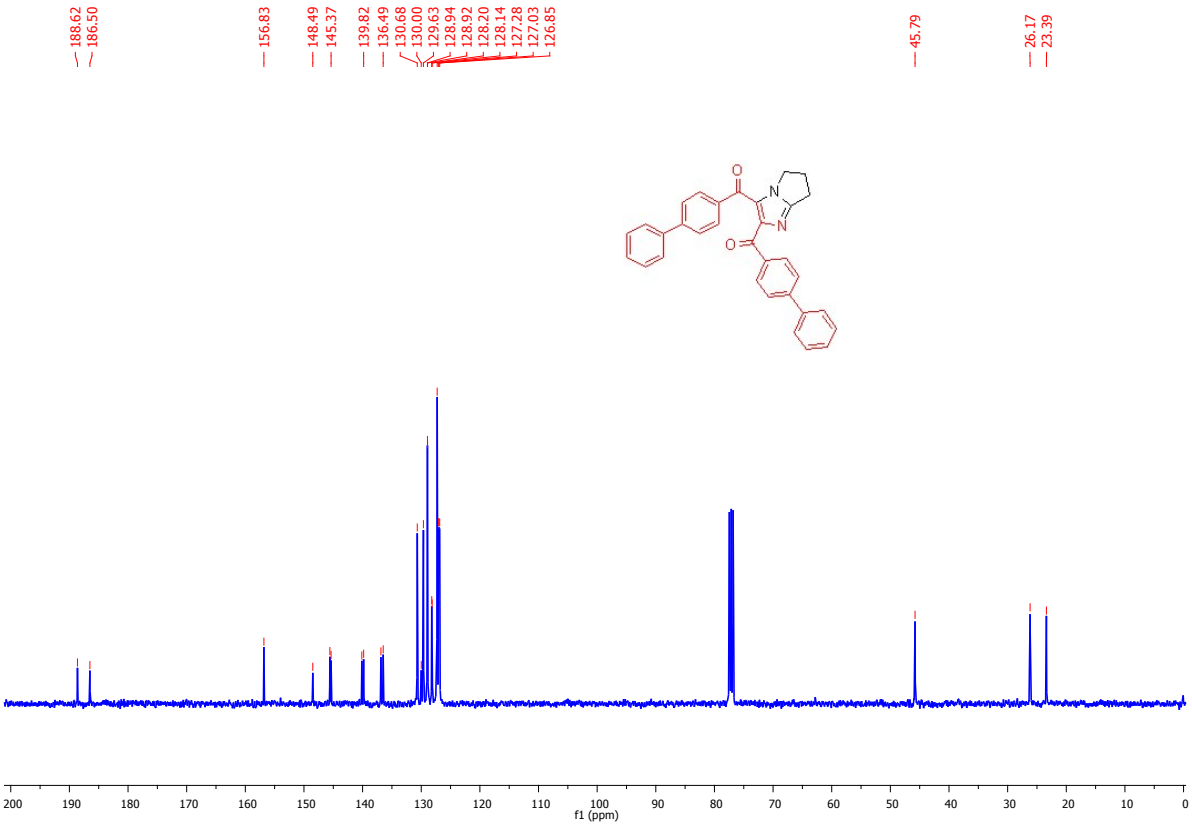
^{1}H NMR spectrum of **5b** (500 MHz, $CDCl_3$)



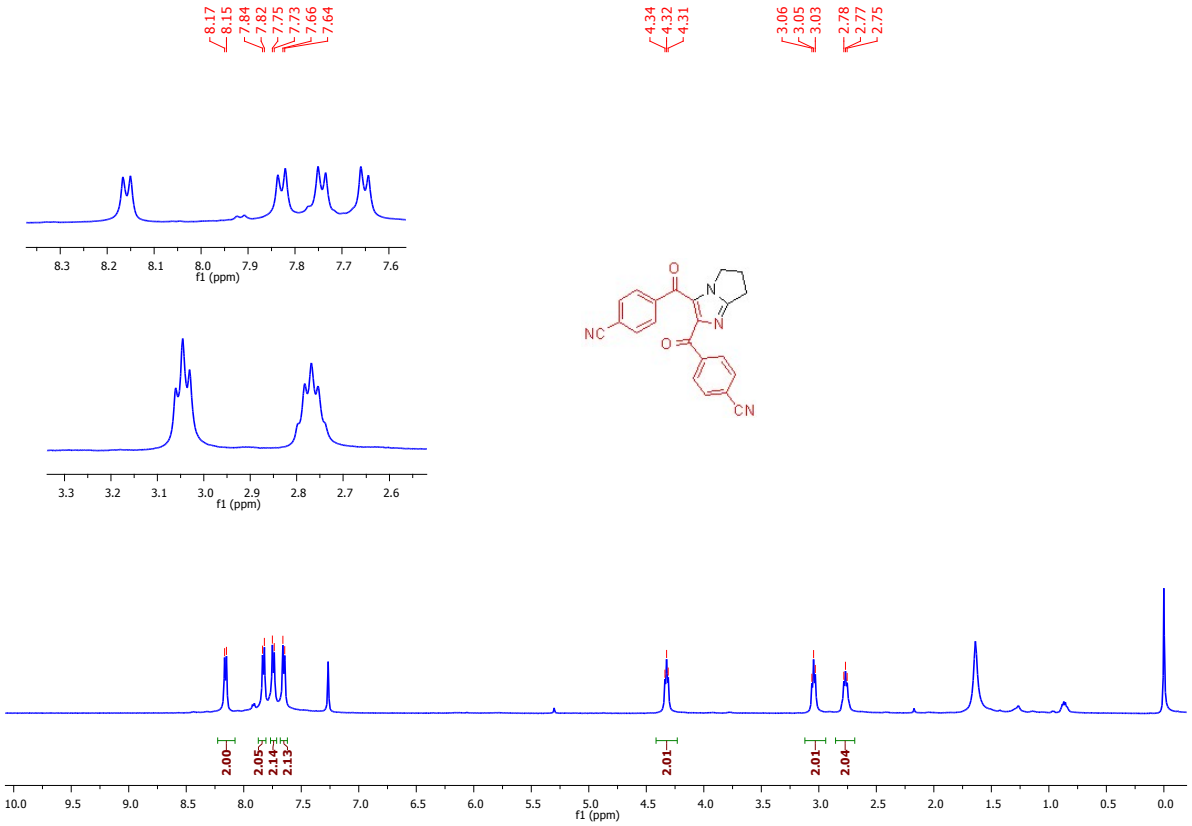
^{13}C NMR spectrum of **5b** (100 MHz, $CDCl_3$)



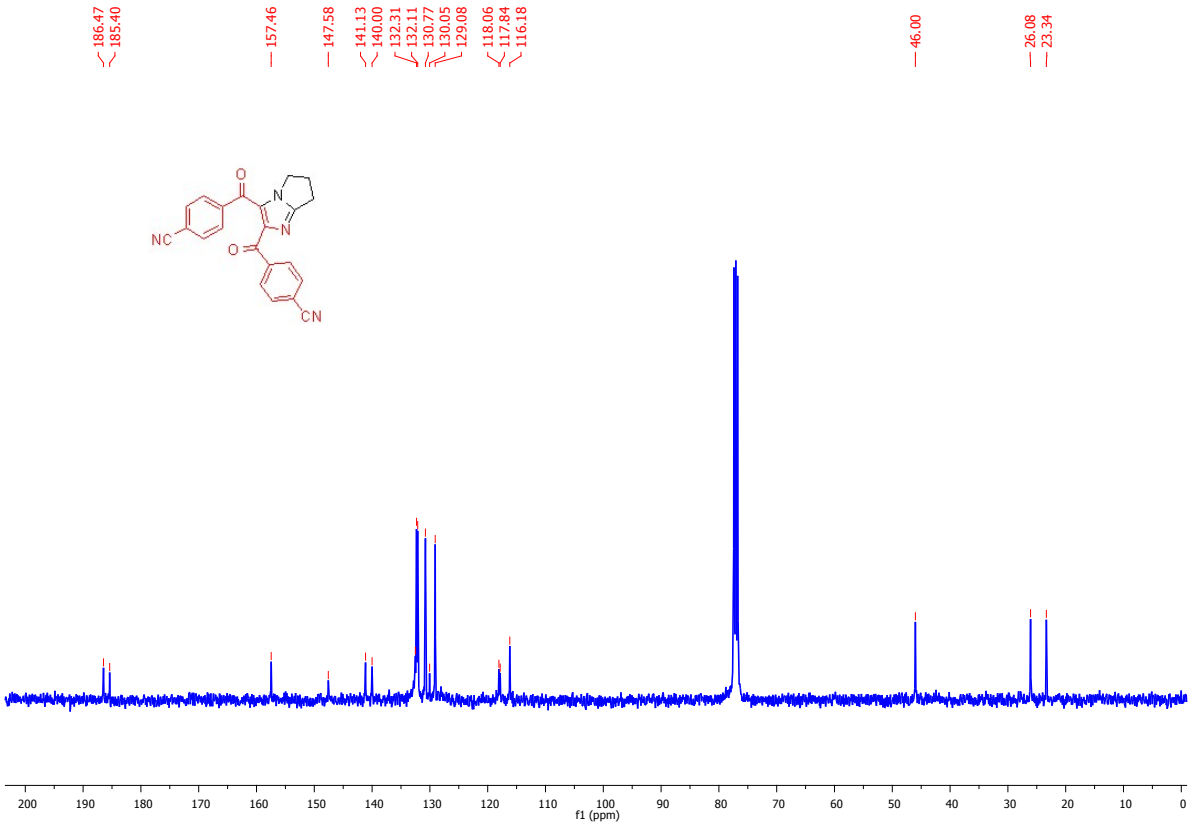
^{1}H NMR spectrum of **5c** (500 MHz, $CDCl_3$)



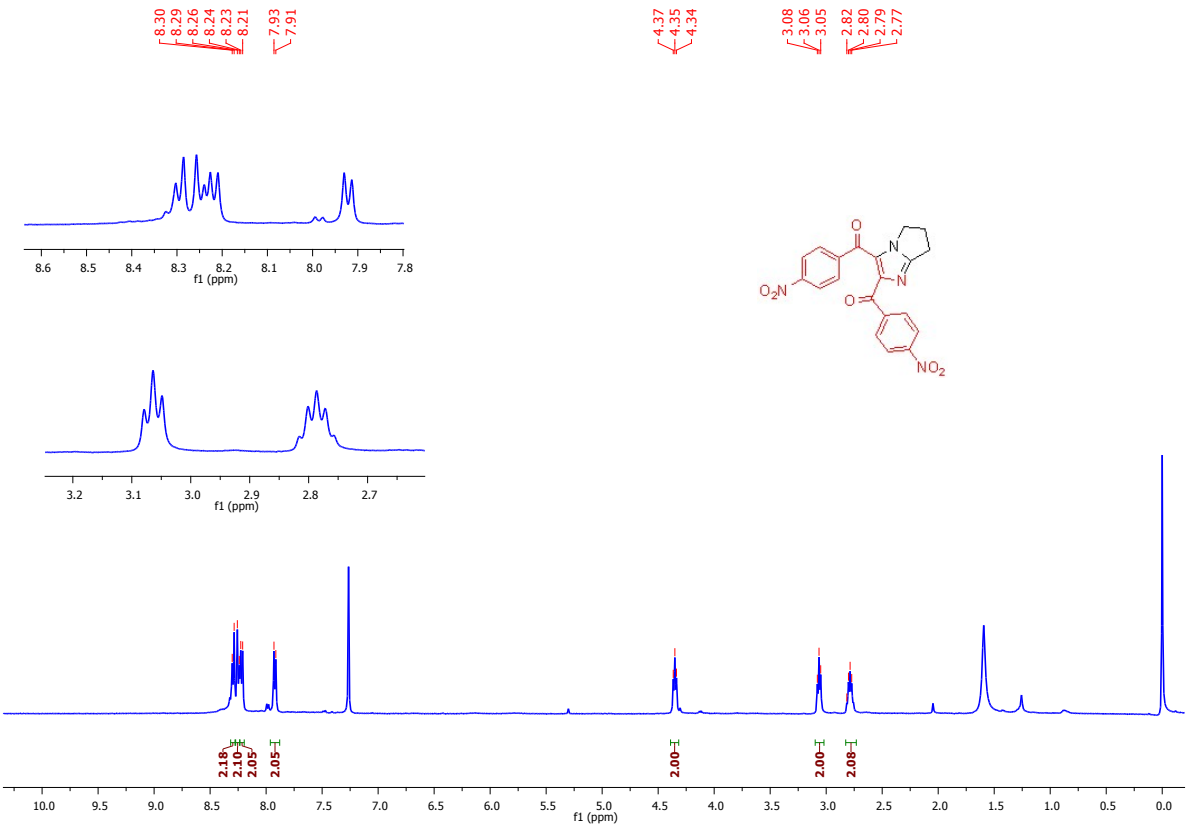
^{13}C NMR spectrum of **5c** (100 MHz, $CDCl_3$)



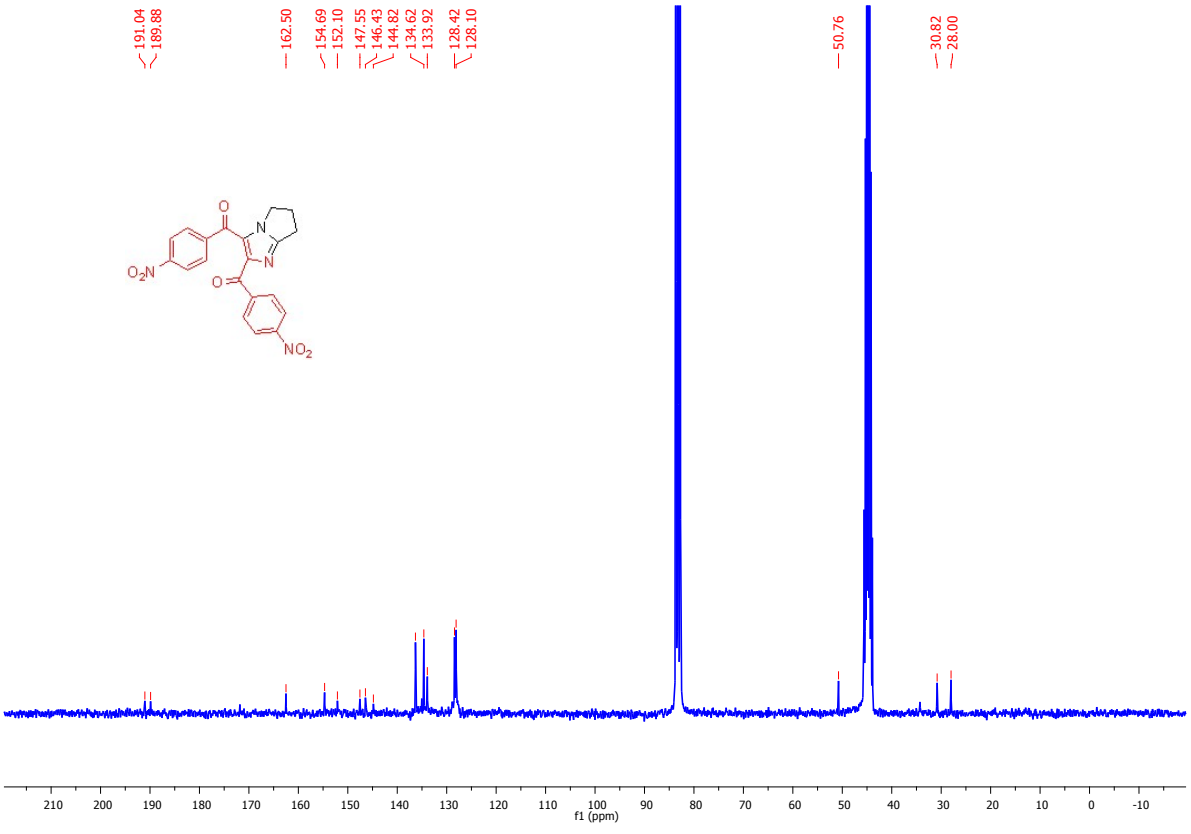
^{1}H NMR spectrum of **5d** (500 MHz, $CDCl_3$)



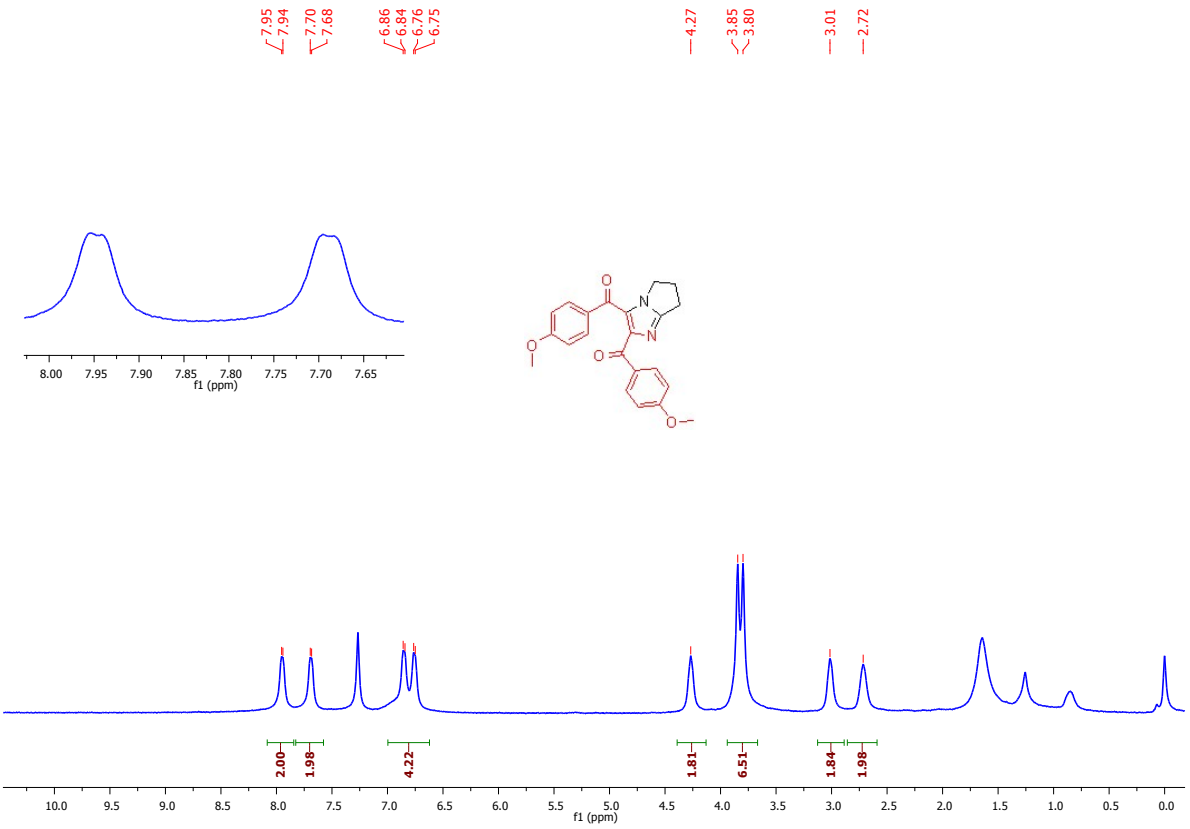
^{13}C NMR spectrum of **5d** (100 MHz, $CDCl_3$)



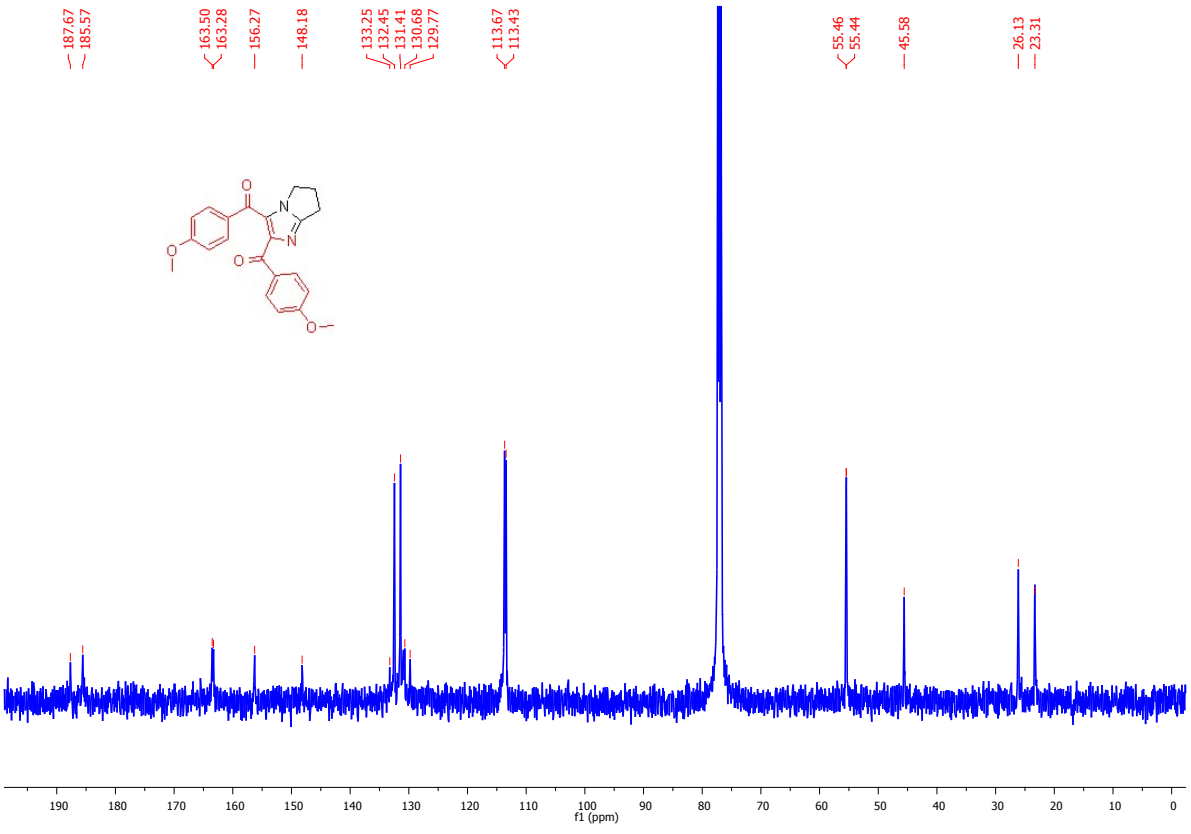
^{1}H NMR spectrum of **5e** (500 MHz, $CDCl_3$)



^{13}C NMR spectrum of **5e** (75 MHz, $CDCl_3$+$DMSOd_6$)



^{1}H NMR spectrum of **5f** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **5f** (125 MHz, $CDCl_3$)